Functional morphology of kidneys
Clearance
Counter-Current System

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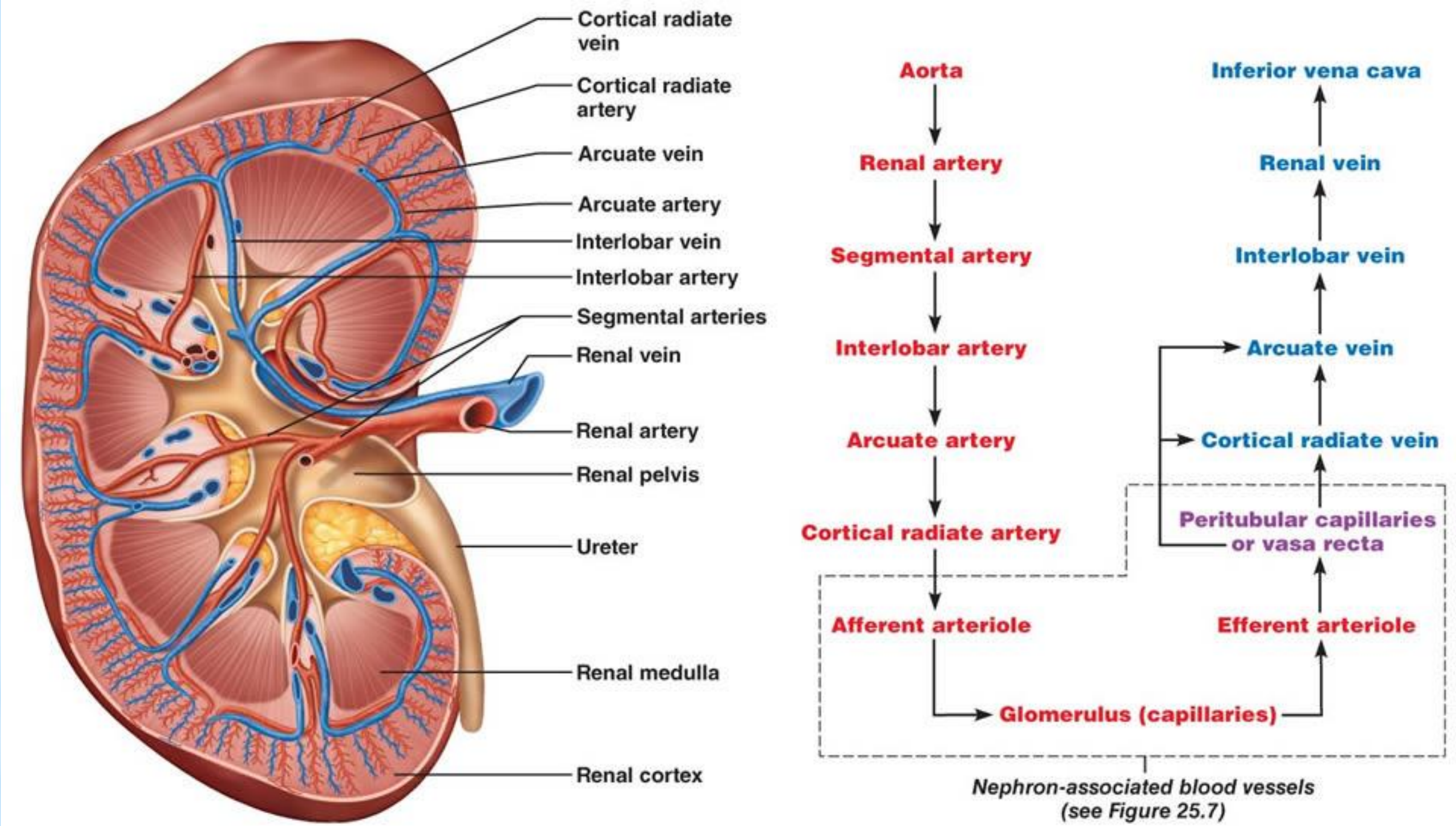
This presentation includes only the most important terms and facts. Its content by itself is not a sufficient source of information required to pass the Physiology exam.

Renal Functions

- Excretion of Waste Products and Toxins
  (entry from the external environment or production in the course of metabolic events)
- Control of Volume and Composition of Body Fluids, Osmolality
- Regulation of Acid-Base Balance
- Regulation of Blood Pressure
- Secretion, metabolism and excretion of hormones
  (renin, erythropoetin, kinins, prostaglandins, 1,25-diOHcholekalciferol)
- Glukoneogenesis

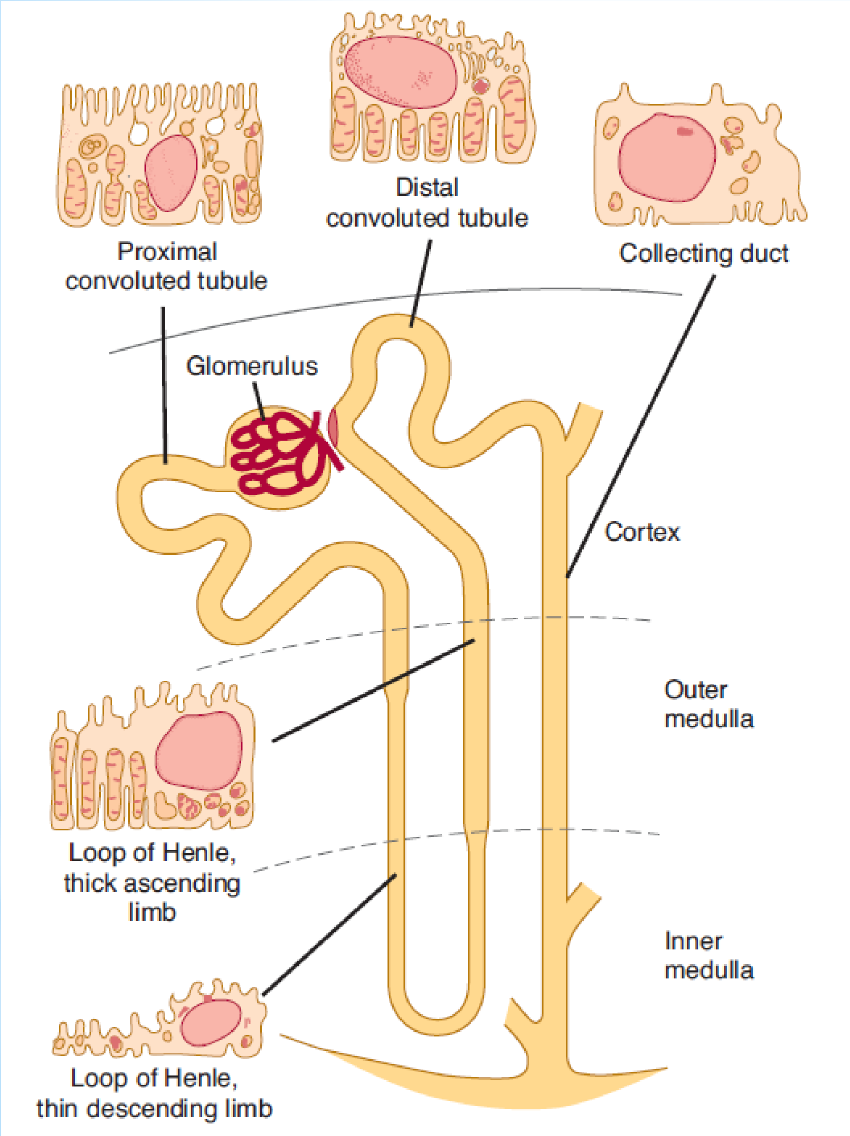
Structure of Kidney



(a) Frontal section illustrating major blood vessels **(b) Path of blood flow through renal blood vessels**

http://classes.midlandstech.edu/carterp/Courses/bio211/chap25/chap25.htm

Structure of Nephron



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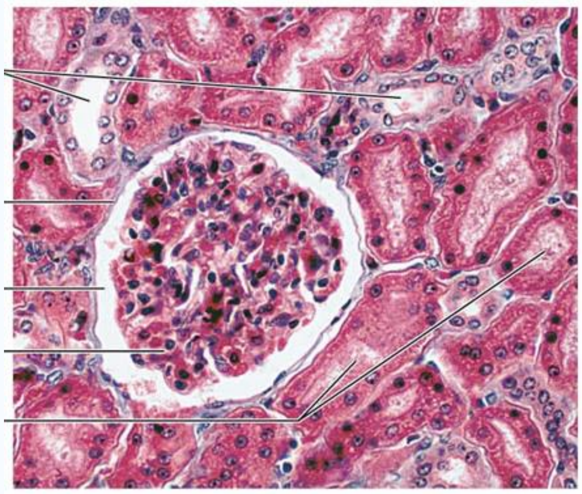
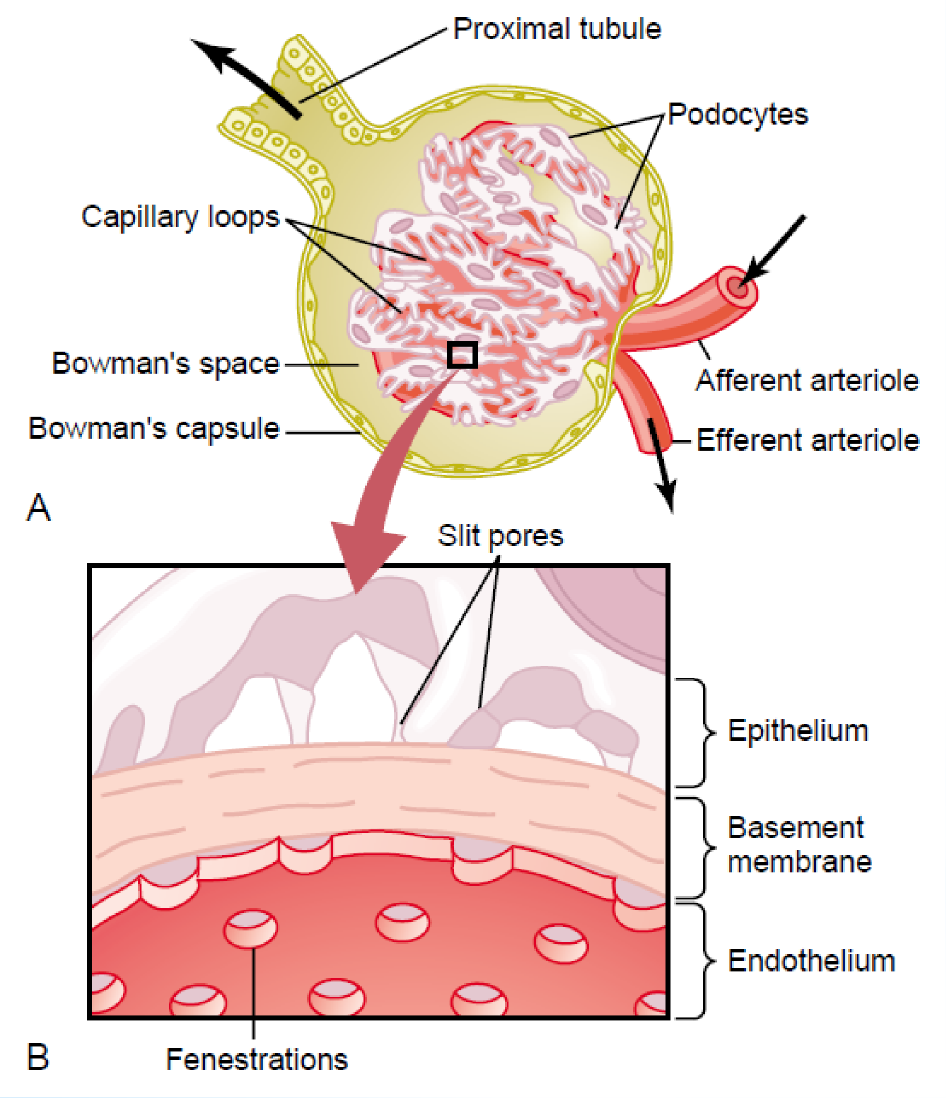
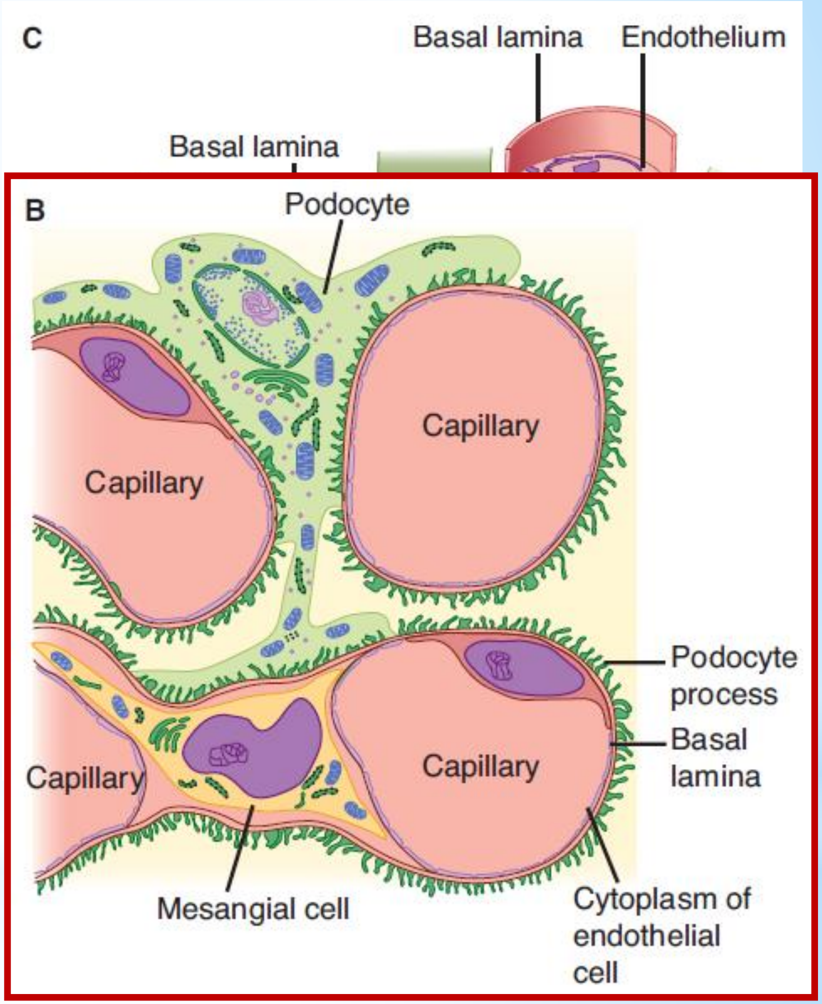


f renal cortical tissue (180×)

Structure of Nephron - Glomerulus





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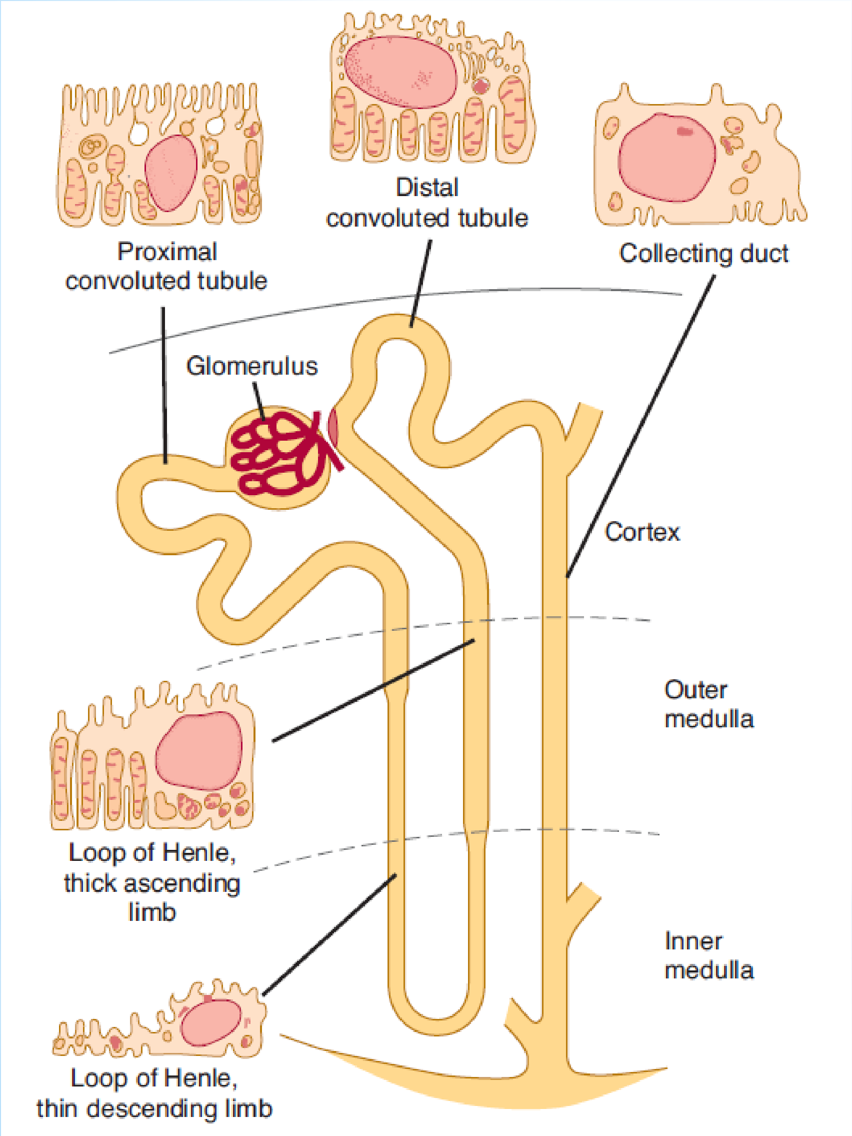
Structure of Nephron - Tubulus



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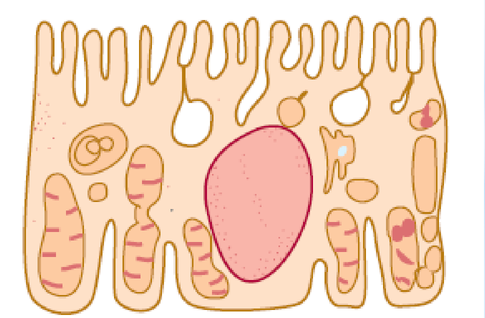
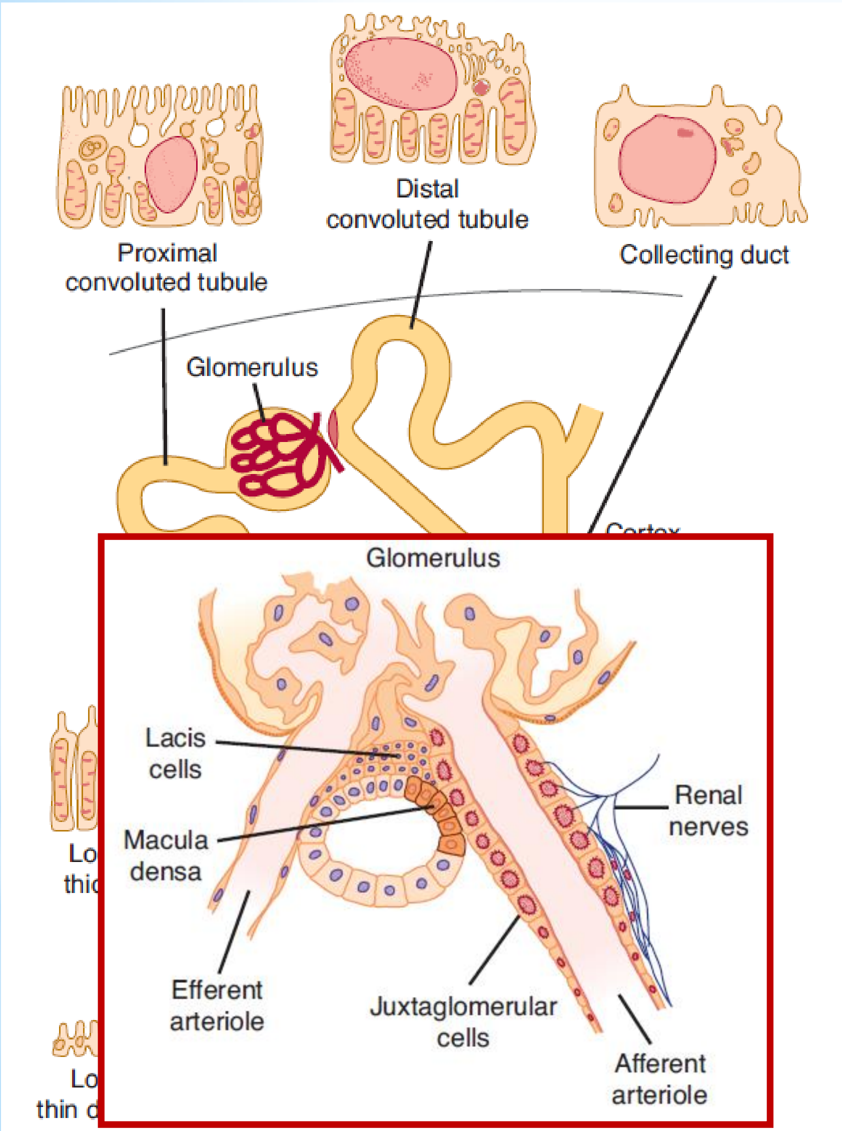
- glomerulus
- proximal convoluted tubule



Structure of Nephron - Tubulus

- glomerulus
- proximal convoluted tubule
- loop of Henle



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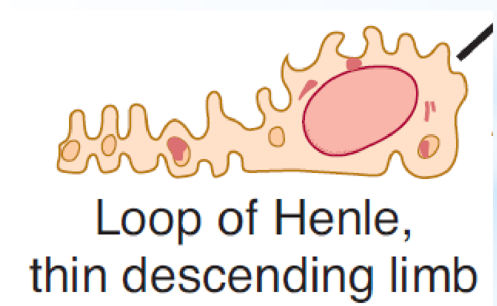
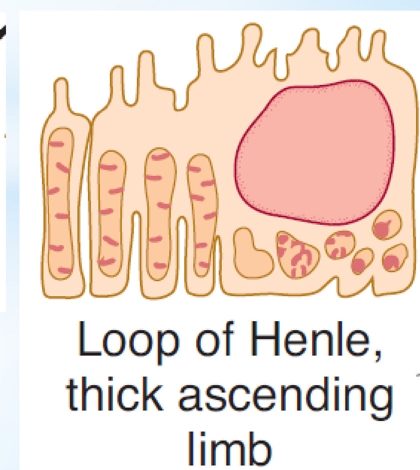
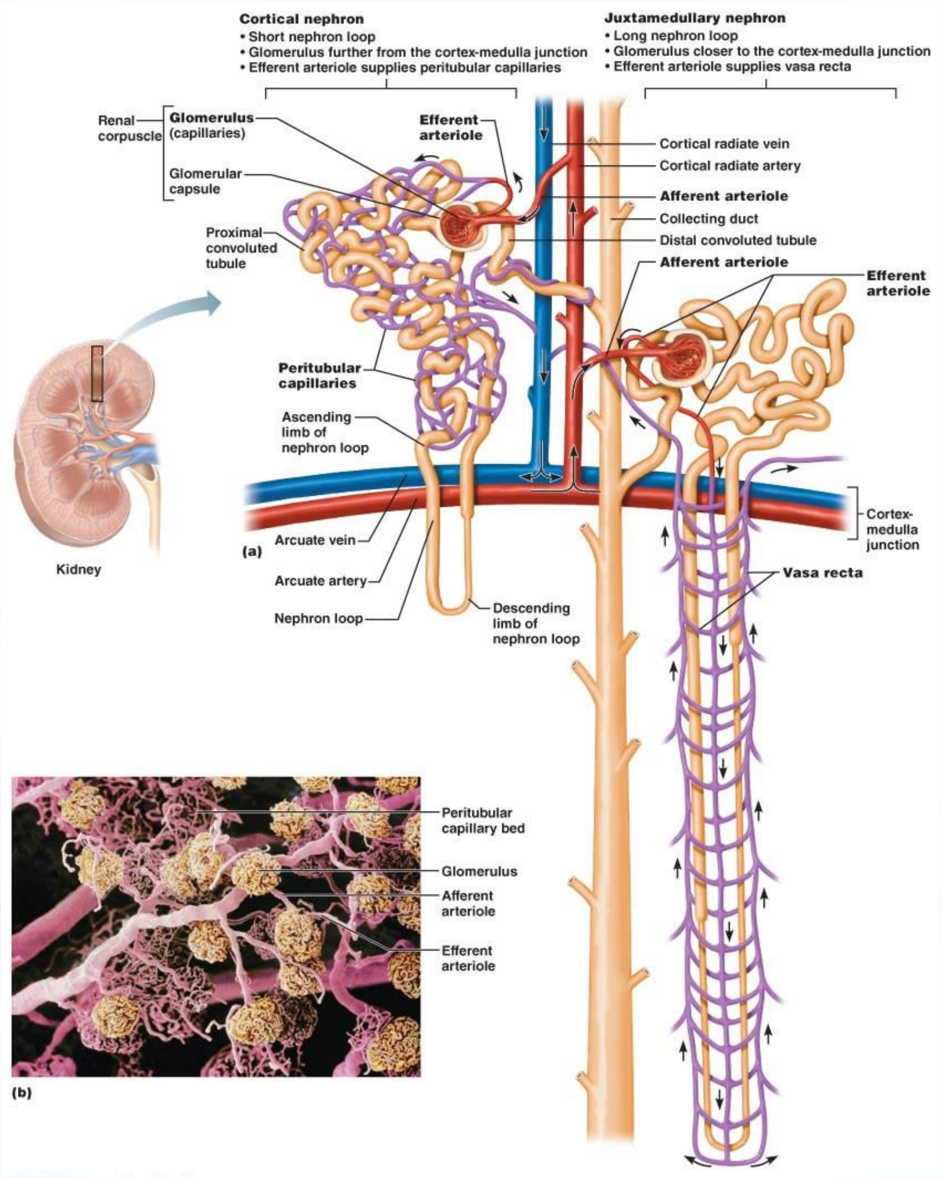




Structure of Nephron - Tubulus



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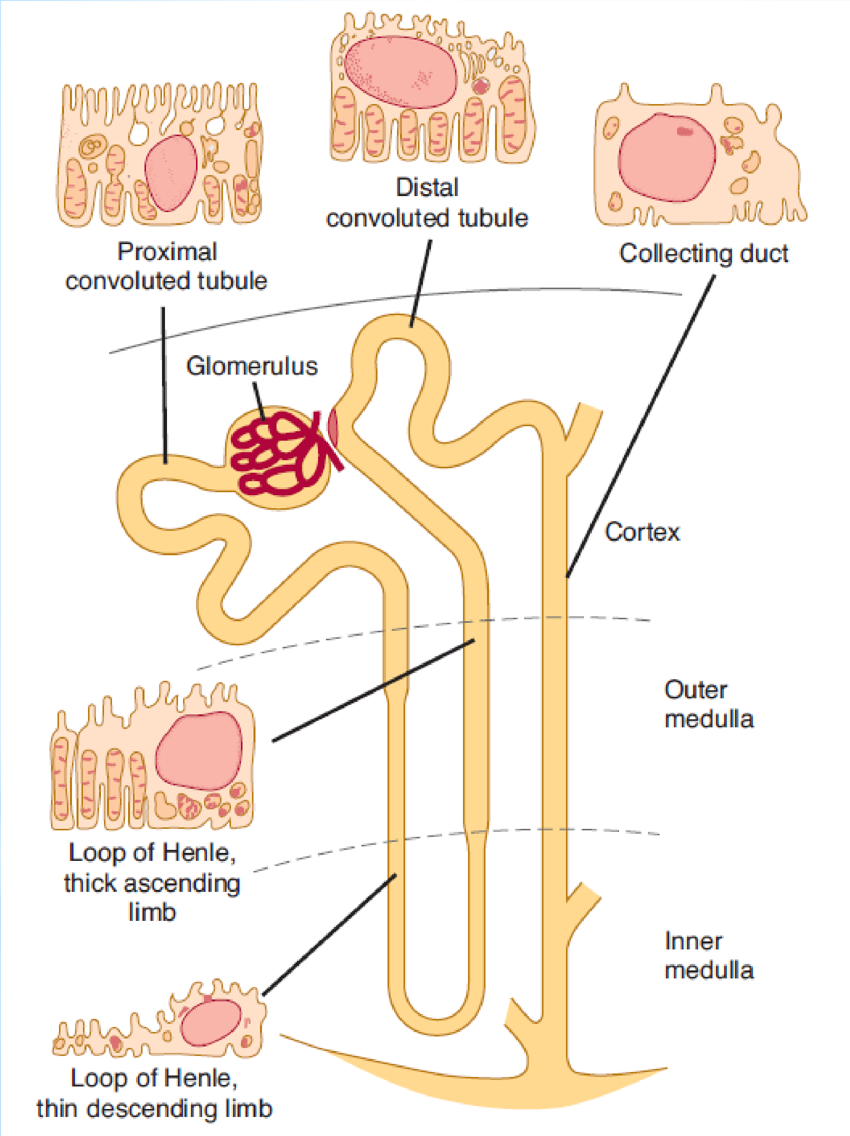
Structure of Nephron - Tubulus



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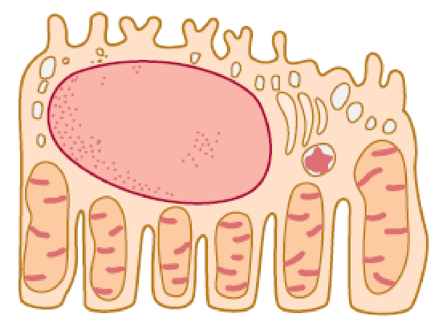
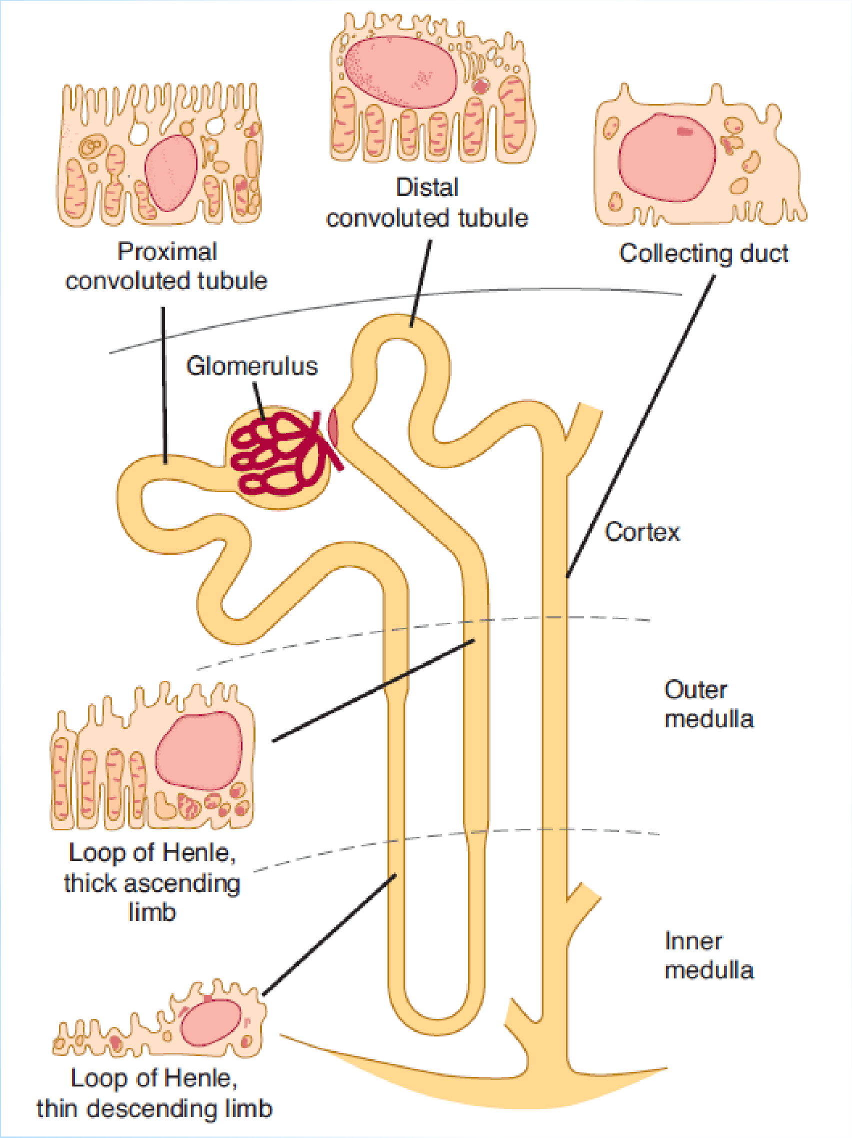
- glomerulus
- proximal convoluted tubule
- loop of Henle
- distal convoluted tubule



Distal
convoluted tubule

Structure of Nephron - Tubulus



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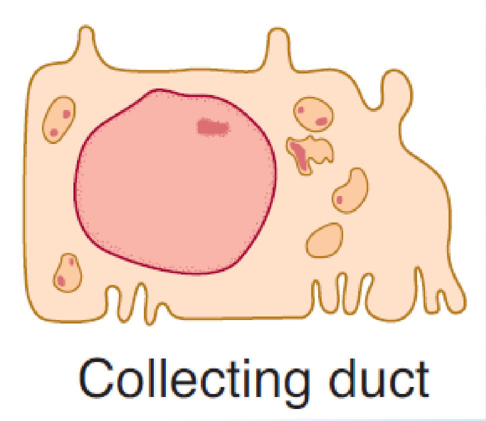
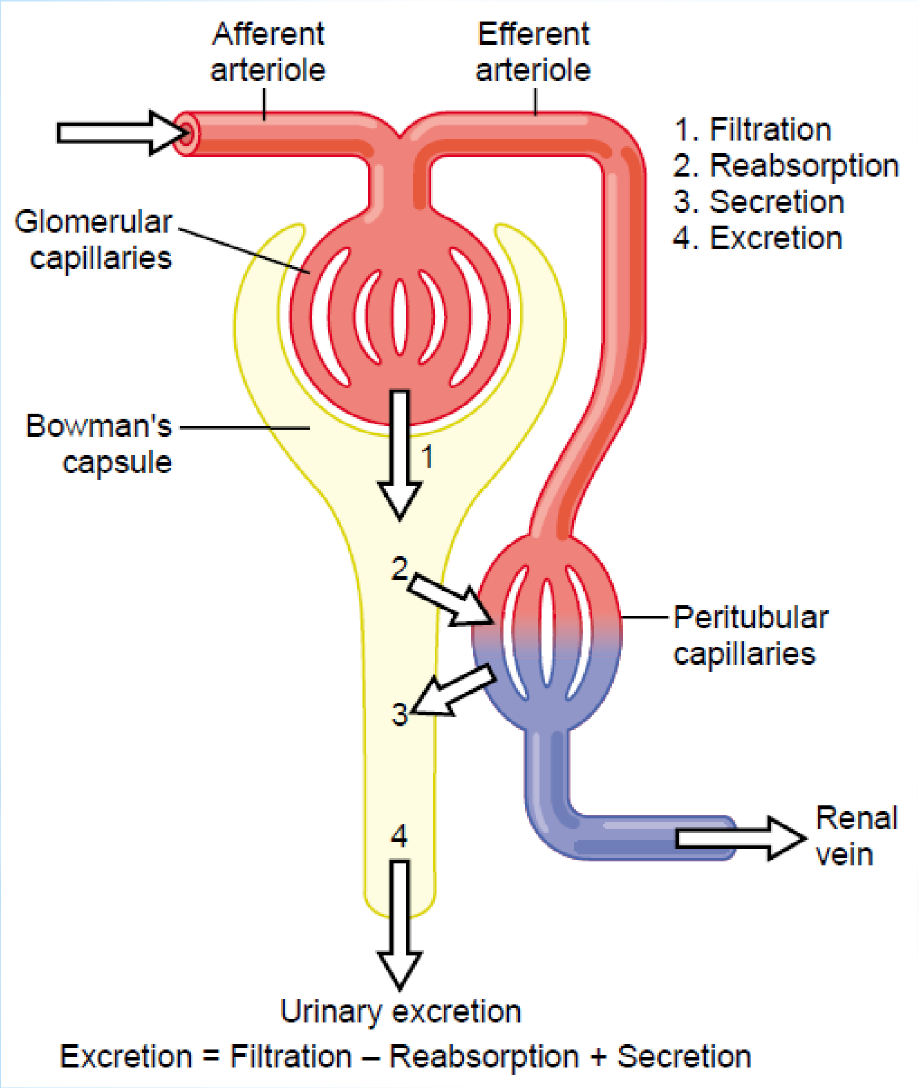
- glomerulus
- proximal convoluted tubule
- loop of Henle
- distal convoluted tubule
- collecting duct



Urine Formation



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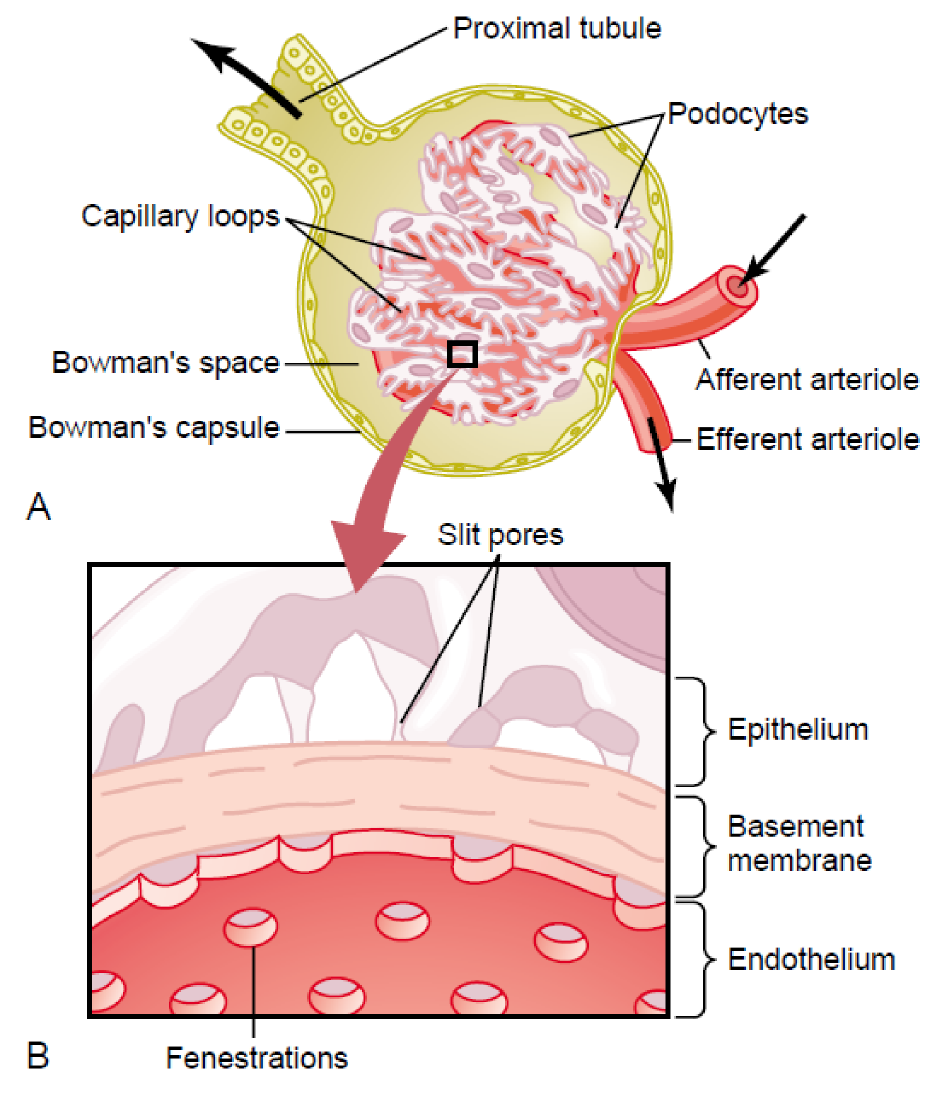
1) Glomerular filtration
2) Tubular reabsorption
3) Tubular secretion
4) Urine excretion

Urine Formation - Glomerular Filtration



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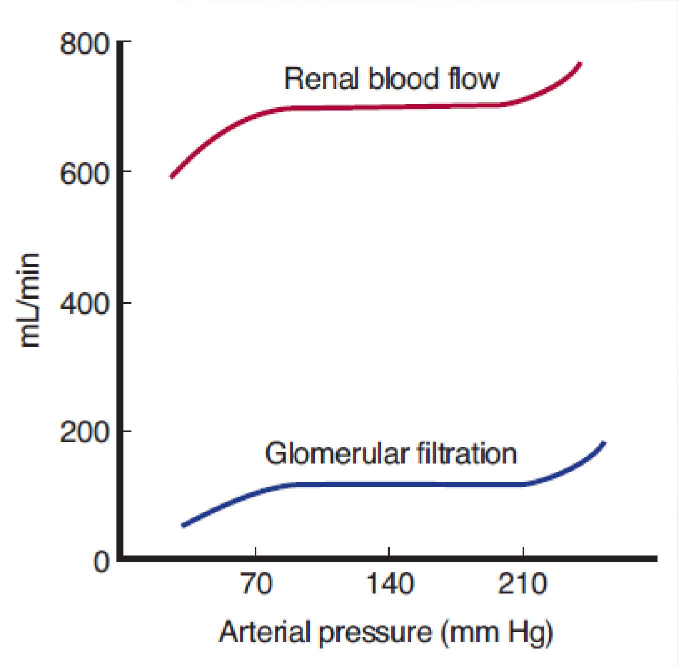
GFR = 125 ml/min = 180 l/day

FF = 0.2

20% of plasma filtered!



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Urine Formation - Glomerular Filtration

Glomerular filtration rate (GFR) depends on:

1) Capillary filtration coefficient K_f
   (permeability and area of glomerular membrane)

2) Balance of hydrostatic and coloid osmotic forces

$$GFR = K_f \cdot \text{net filtration pressure}$$

Urine Formation - Glomerular Filtration

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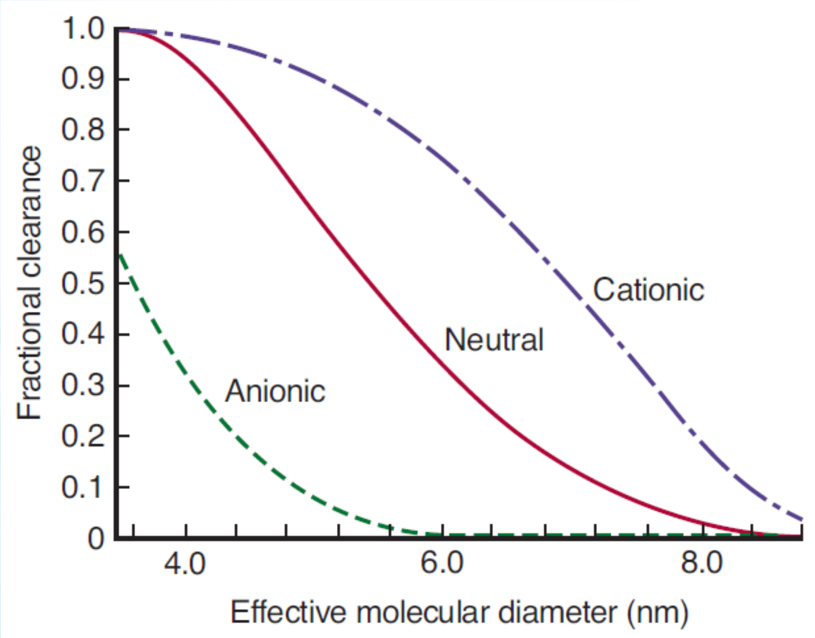
Permeability



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albumin: diameter ~7 nM

loss of negative membrane charge
↓
proteinuria (albuminuria)

Urine Formation - Glomerular Filtration

Glomerular filtration rate (GFR) depends on:

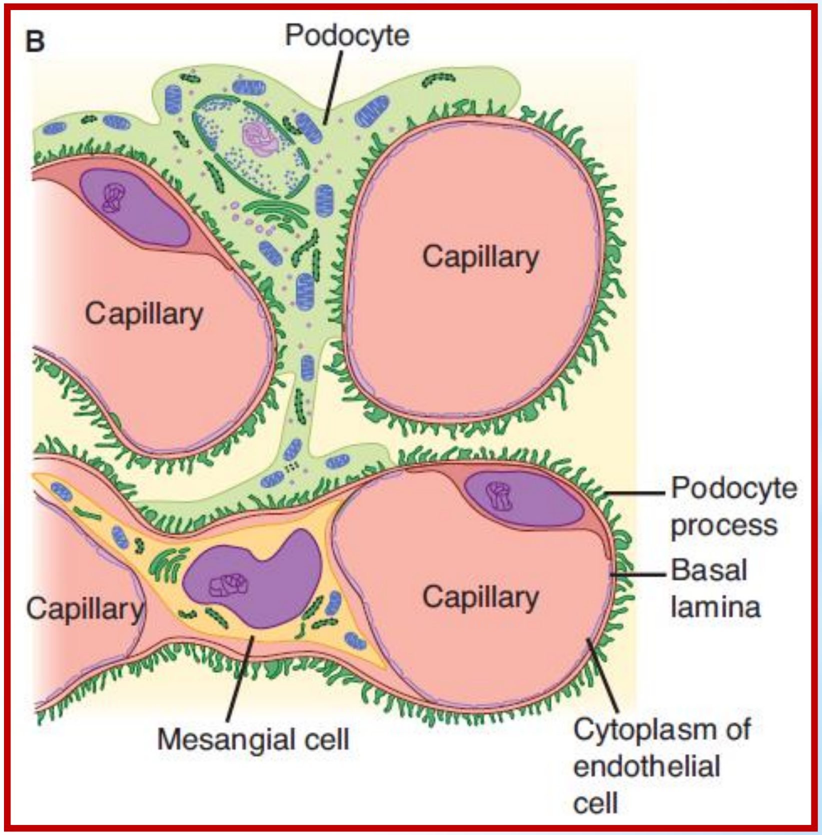
1) Capillary filtration coefficient K_f
(permeability and area of glomerular membrane)

Permeability

Area of capillary bed

mesangial cells:

contraction → reduction of filtration area → ↓ K_f → ↓ GFR



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Permeability

Area of capillary bed

mesangial cells:

contraction → reductio
of filtration area → ↓ K
→ ↓ GFR

Contraction	Relaxation
Endothelins	ANP
Angiotensin II	Dopamine
Vasopressin	PGE_2
Norepinephrine	cAMP
Platelet-activating factor	
Platelet-derived growth factor	
Thromboxane A_2	
PGF_2	
Leukotrienes C_4 and D_4	
Histamine	

Urine Formation - Glomerular Filtration

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Urine Formation - Glomerular Filtration

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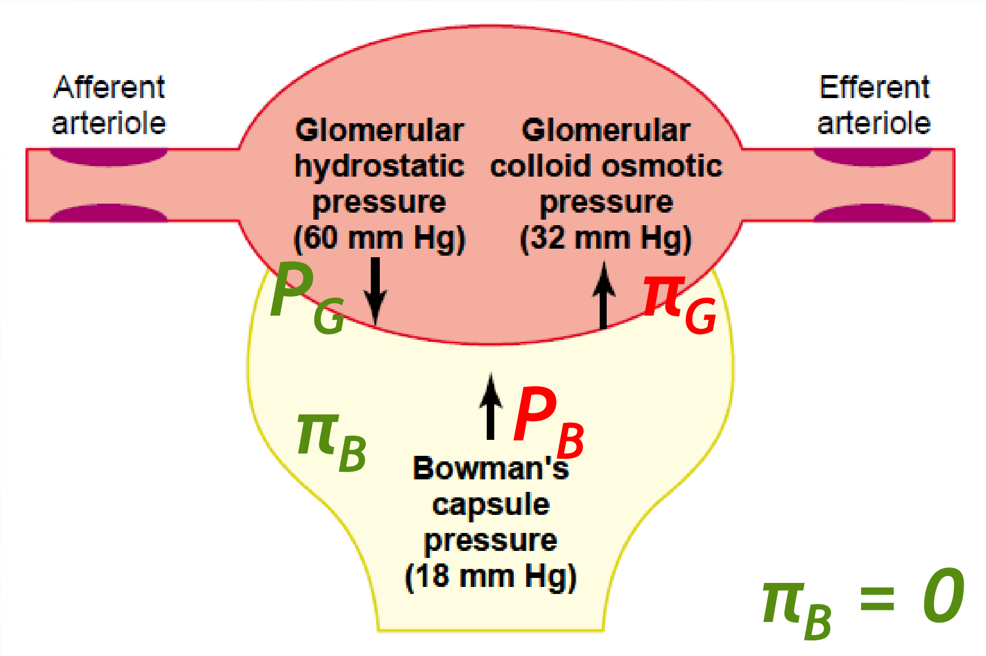

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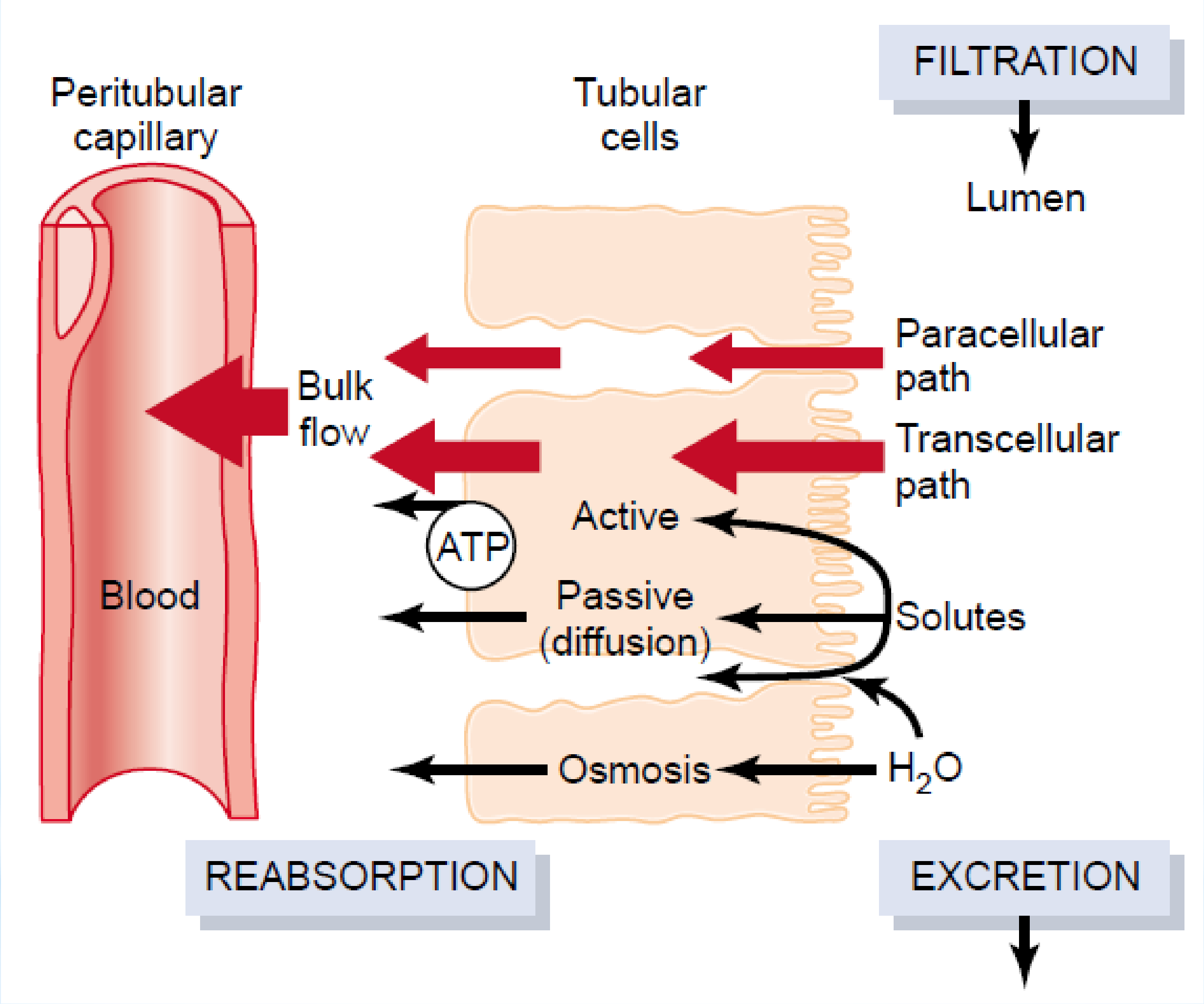
Under physiological conditions:

net filtration pressure = $P_G + \pi_B - P_B - \pi_G = 60 + 0 - 18 - 32 = 10$ mmHg

$$GFR = K_f \cdot (P_G + \pi_B - P_B - \pi_G)$$

Urine Formation – Tubular Processes



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Urine Formation – Tubular Processes

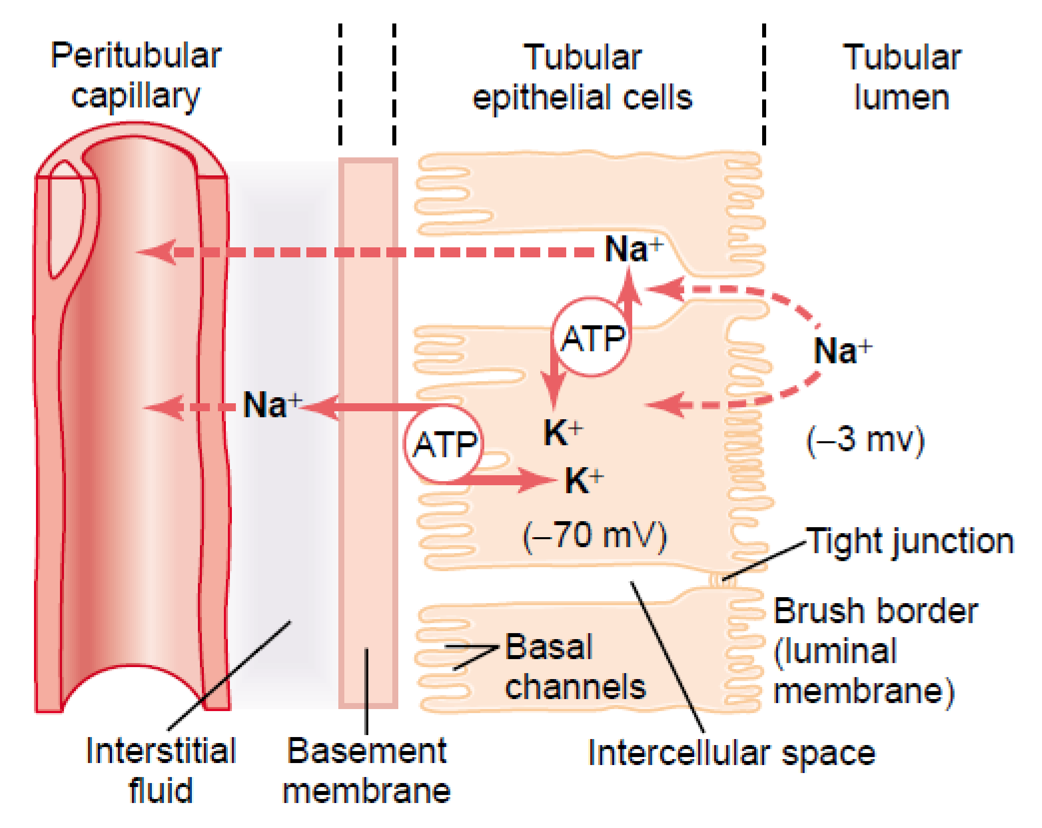
Active Transport Mechanisms

1) Primary active transport
2) Secondary active transport
3) Pinocytosis
   (big molecules, *e.g.* proteins, namely in the proximal tubule)

Urine Formation – Tubular Processes

Active Transport Mechanisms

1) Primary active transport



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Urine Formation – Tubular Processes

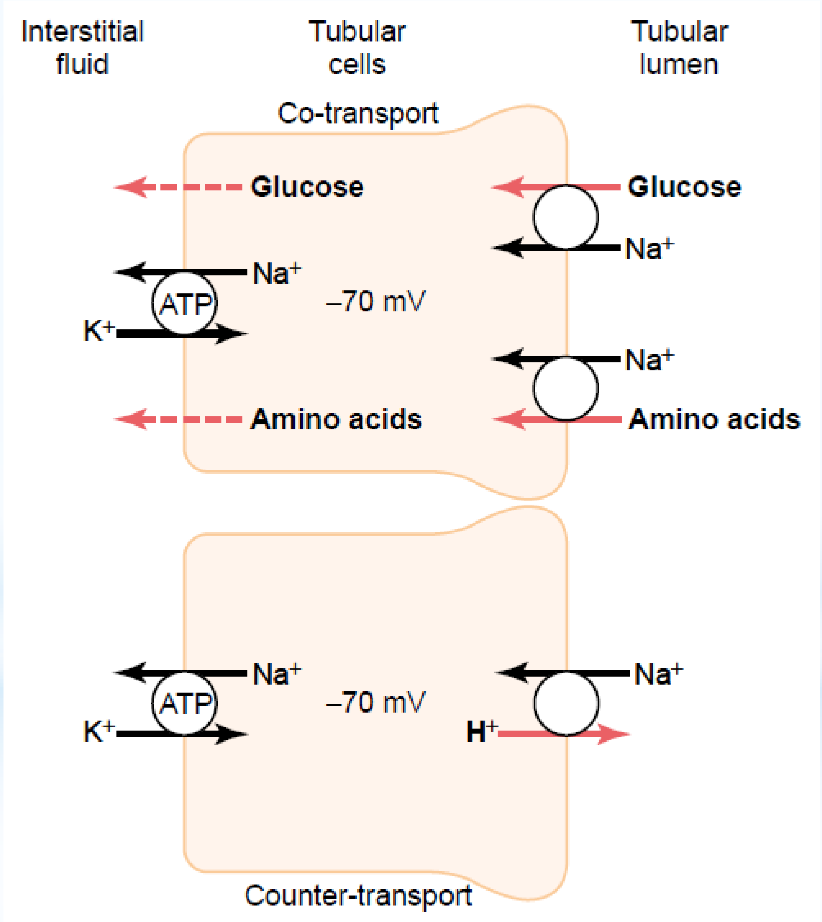
Active Transport Mechanisms

1) Primary active transport
   - Na^+/K^+ ATPase
   - H^+ ATPase
   - Ca^{2+} ATPase

Urine Formation – Tubular Processes

Active Transport Mechanisms

2) Secondary active transport



symport

antiport

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Urine Formation – Tubular Processes

Active Transport Mechanisms

Substances using active transport show the so called transport maximum (given by saturation of the transporter).

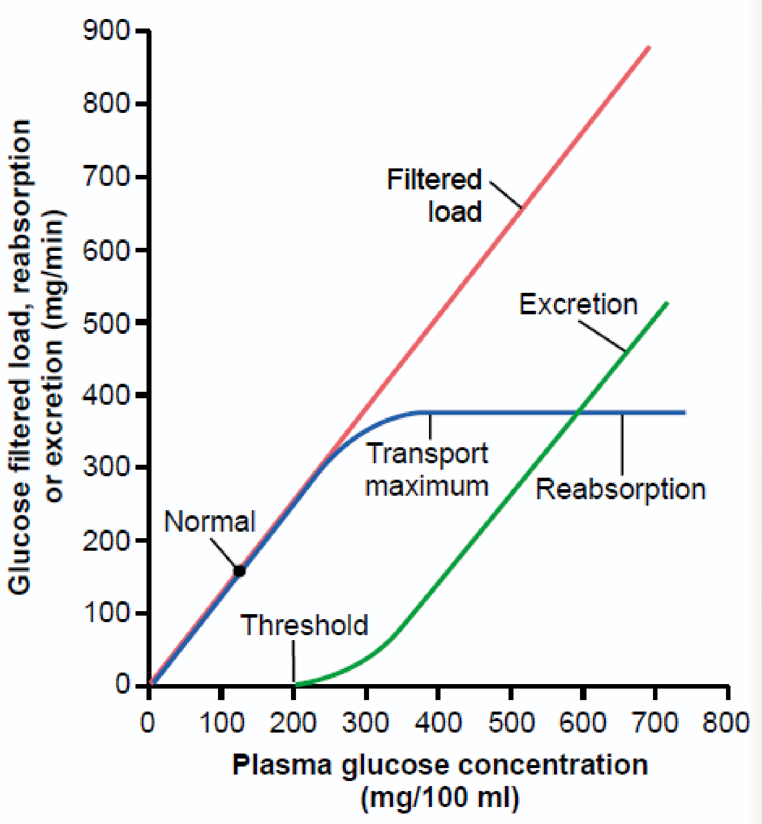
for example glucose

transport maximum:

ženy ~300 mg/min

muži ~375 mg/min

diabetes mellitus



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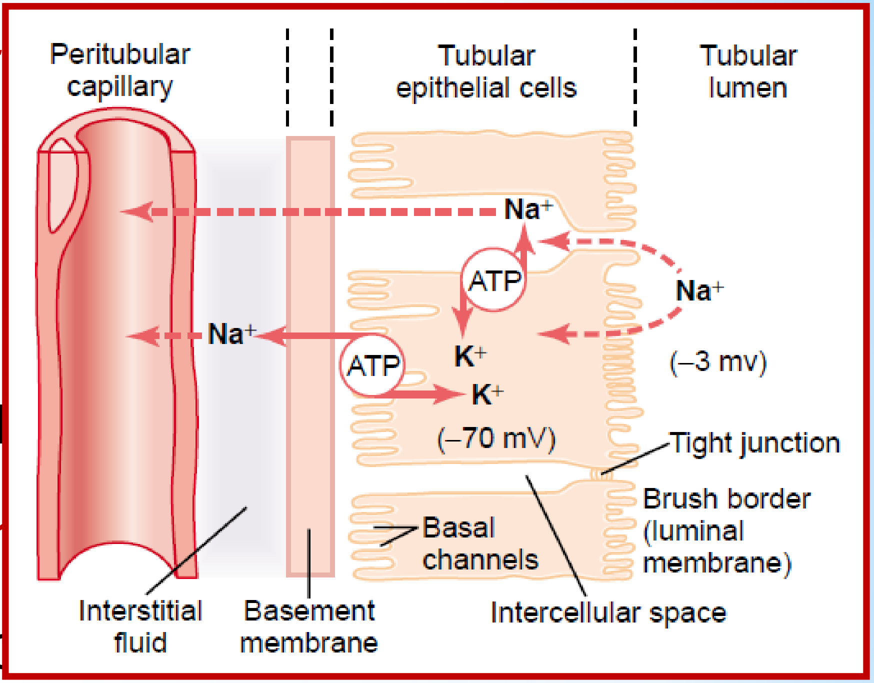
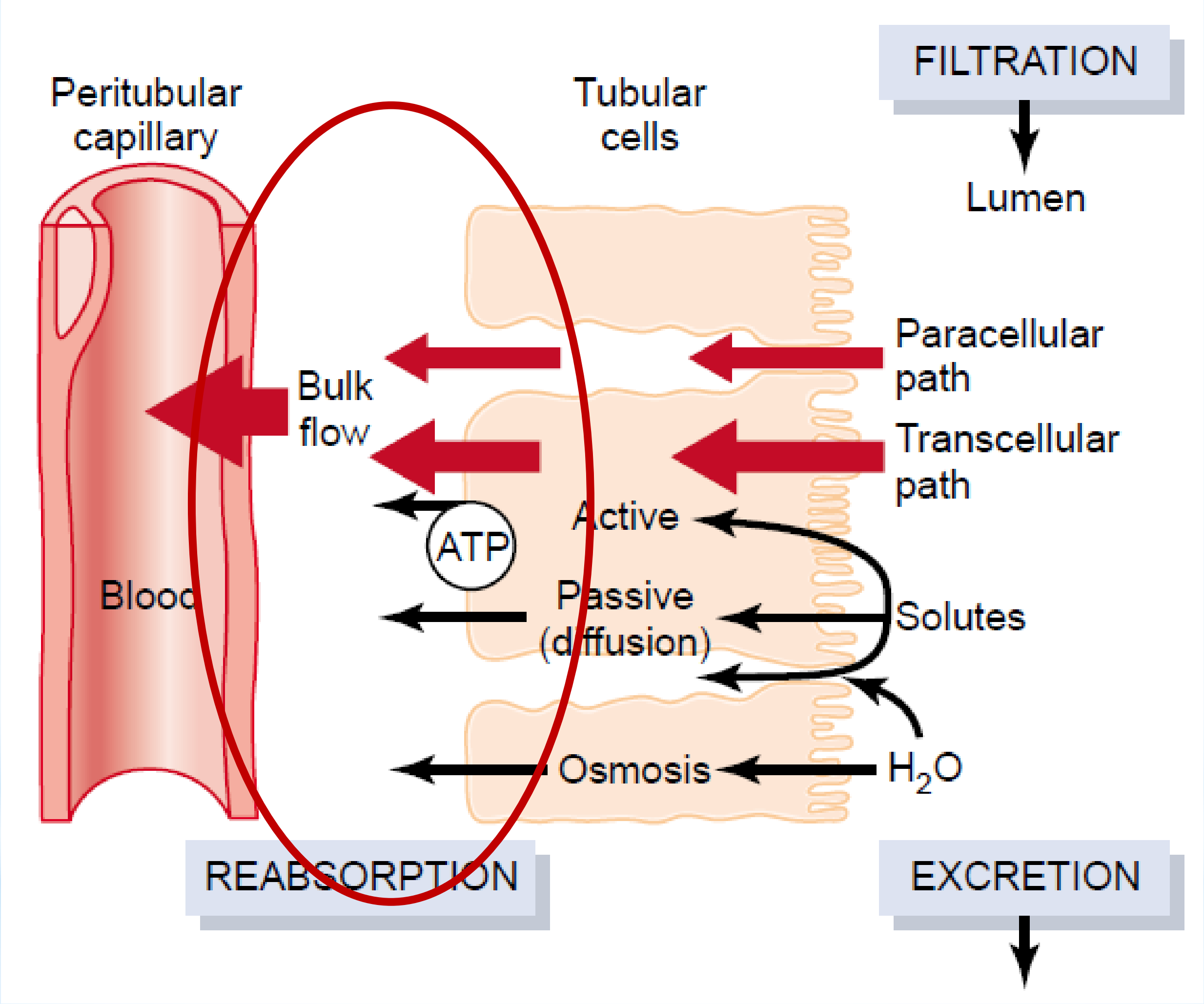


Passive Transpor

1) Reabsorption of H_2O by osmo
   - in the proximal tubule (highly permeable for H_2O)
   - active reabsorption of solutes → lumen-intersticium concentration gradient → H_2O osmosis into intersticium
2) Reabsorption of solutes by diffusion
   - Cl^- (Na^+ into intersticium, reabsorption of H_2O by osmosis)
   - urea (reabsorption of H_2O by osmosis)

Urine Formation – Tubular Processes



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Urine Formation – Tubular Processes

Physical Forces in Peritubular Capillaries and in Renal Intersticium

- tubular reabsorption is controlled by hydrostatic and coloid osmotic forces (similary to GFR)

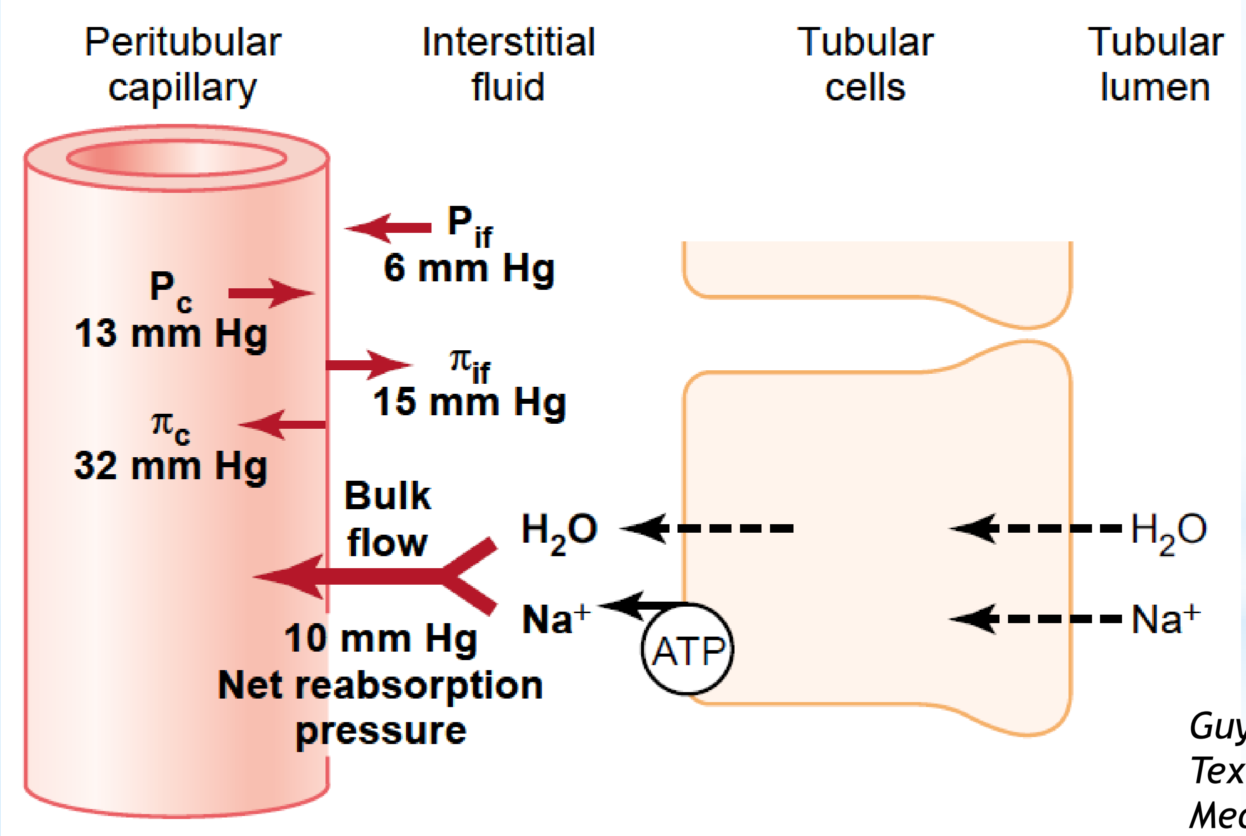
$$GFR = K_f \cdot \text{net filtration pressure}$$

↓

$$TRR = K_f \cdot \boxed{\text{net reabsorptive force}}$$

Urine Formation – Tubular Processes

Physical Forces in Peritubular Capillaries and in Renal Intersticium



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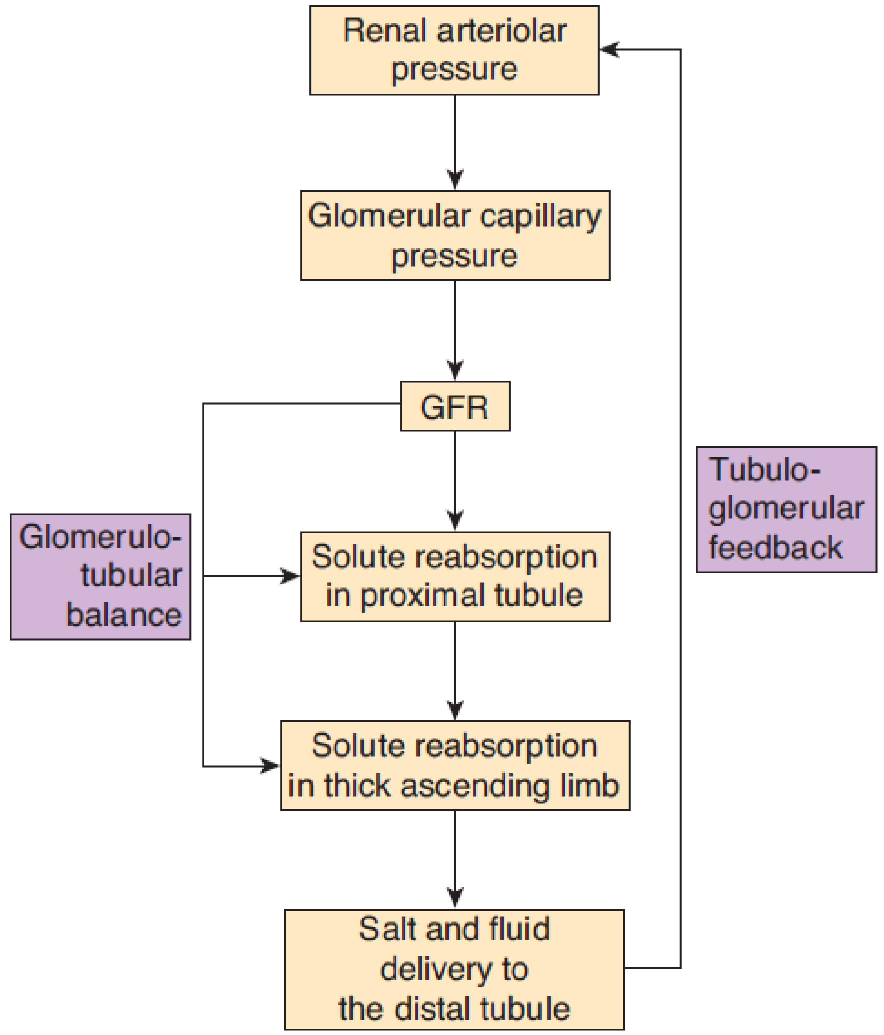
Urine Formation – Tubular Processes

Tubuloglomerular feedback

↑ GFR → ↑ flow of water and solutes to macula densa → constriction of aff. arteriole (tromboxane A2 ?) → ↓ GFR

Glomerulotubular balance

↑ GFR → ↑ oncotic pressure in peritubular capillaries → ↑ reabsorption in tubules



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Urine Formation – Tubular Processes

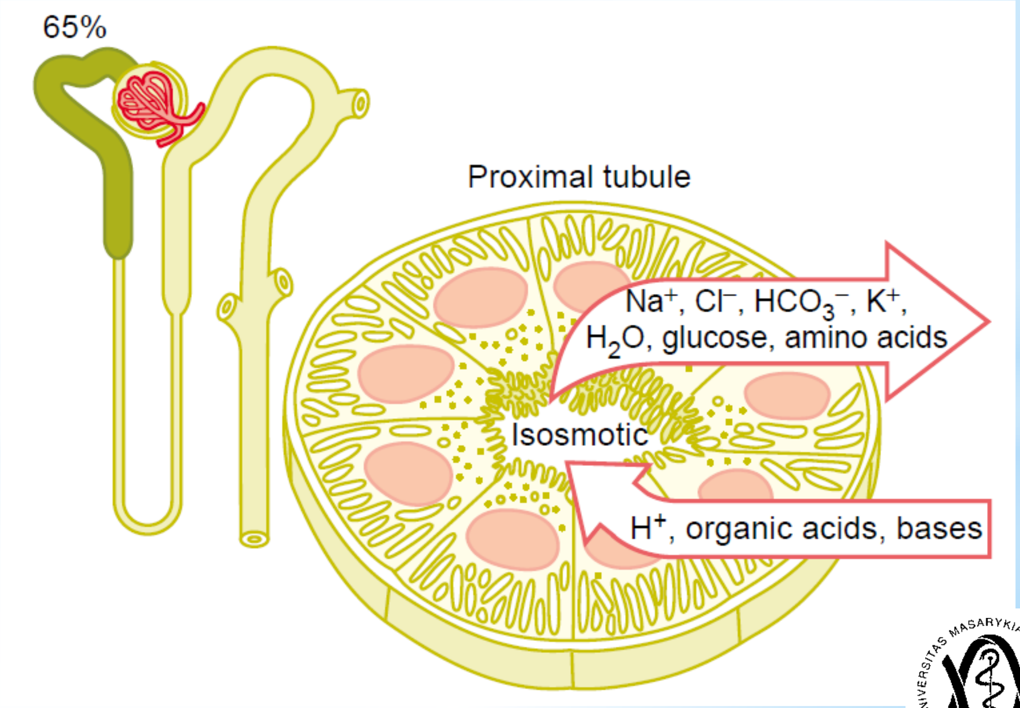
Proximal Tubule

1) complete reabsorption of substances playing key roles for the organism (glucose, amino acids)
2) partial reabsorption of substances important for the organism (ions – Na^+, K^+, Cl^-, *etc.*)
3) reabsorption of water
4) secretion of H^+
5) reabsorption of HCO_3^-

Result:

isoosmotic fluid,

notably decreased volume



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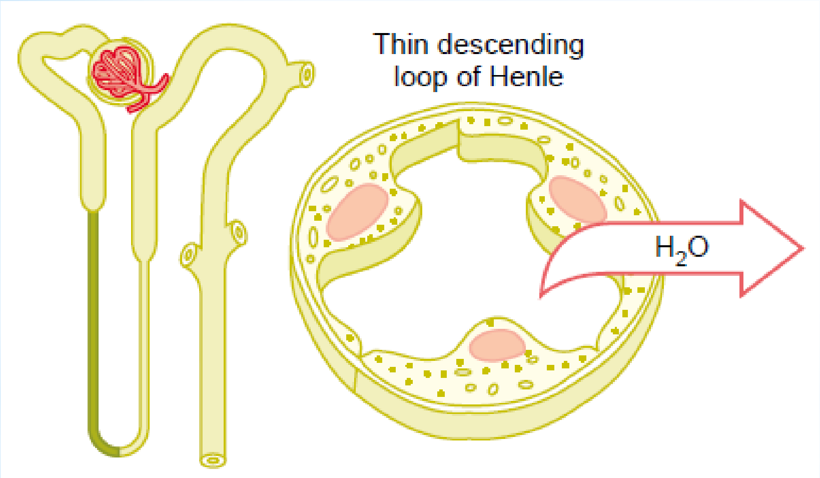
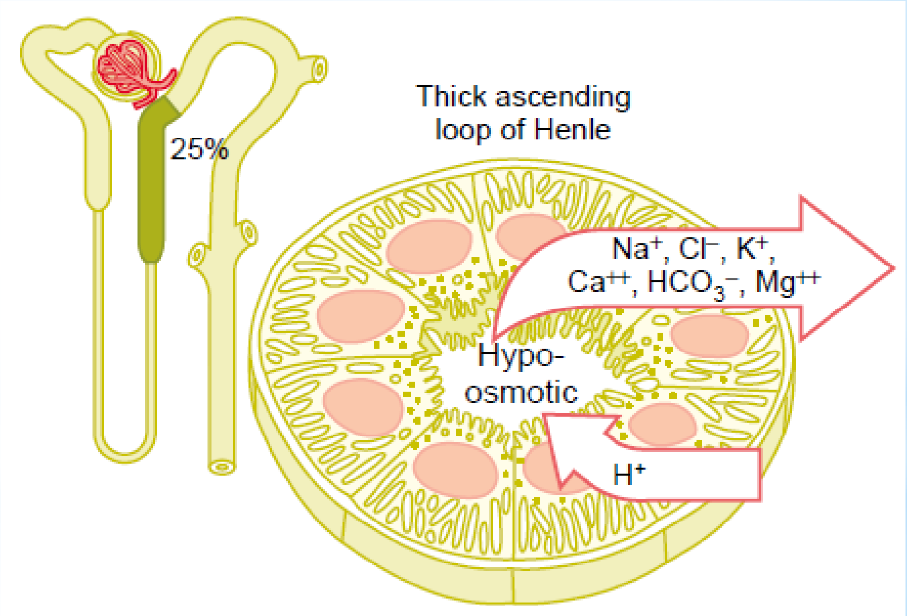
Urine Formation – Tubular Processes

Loop of Henle

1) thin descending part - passive reabsorption of water (osmosis)
2) thick ascending part - active reabsorption of ions ($Na^+/K^+/2Cl^-$ symport), secretion of H^+, reabsorption of HCO_3^-





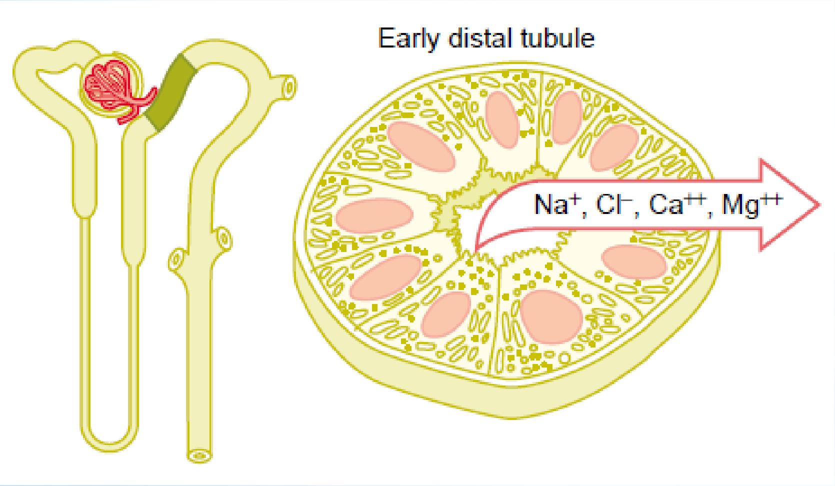
counter-current multiplier

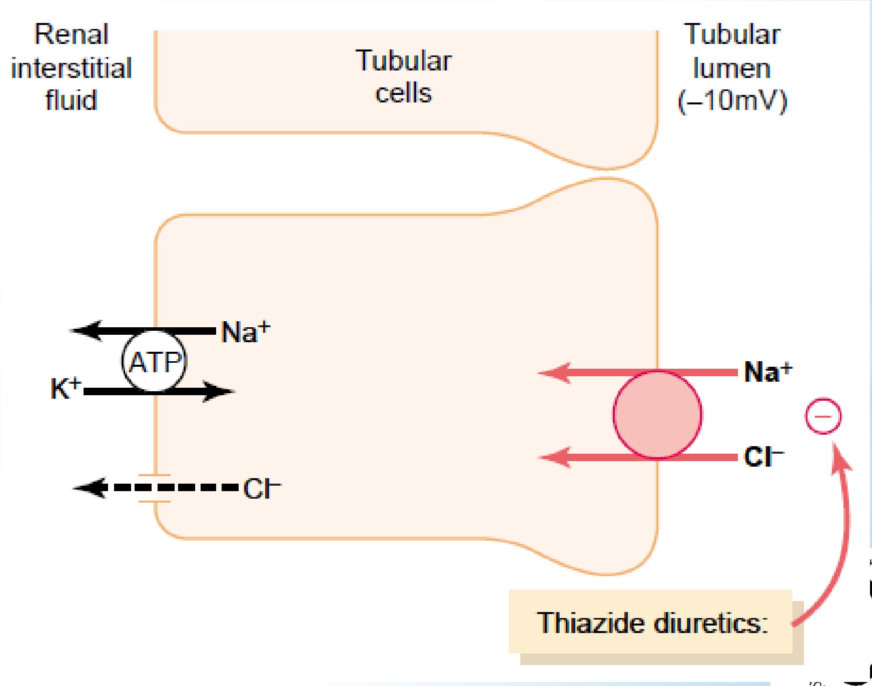
Result: hypotonic fluid, volume further decreased

Urine Formation – Tubular Processes

Distal tubule

1) juxtaglomerular apparatus
2) active reabsorption of solutes similar to the thick ascending loop of Henle, also no permeability for urea and water – the so called dilution segment (dilutes the tubular fluid)



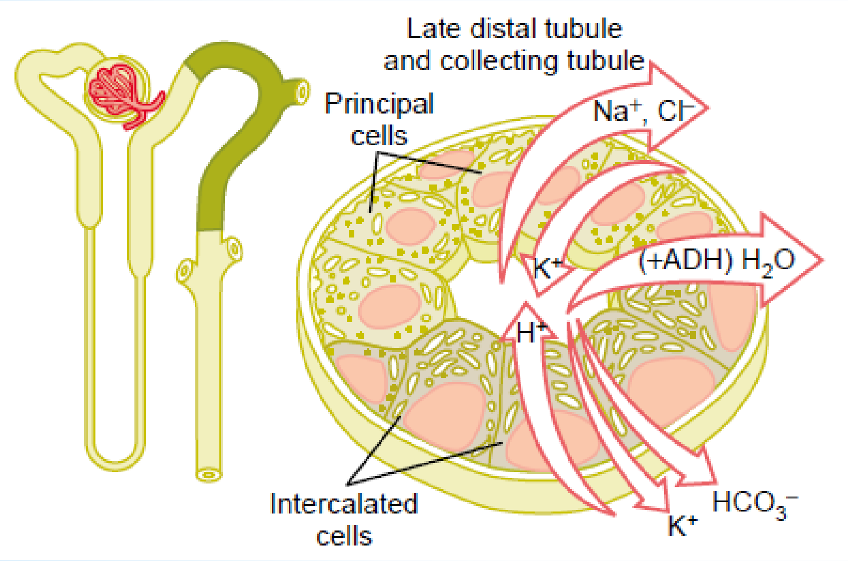


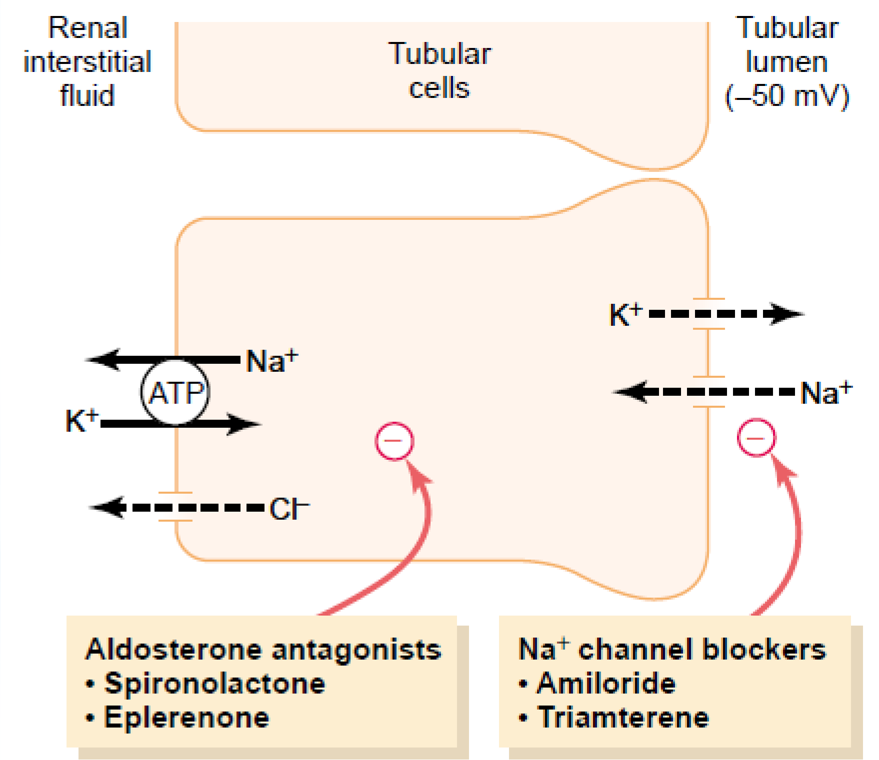
Result: hypotonic fluid

Urine Formation – Tubular Processes

Collecting duct (+ end of distal tubule)

1) principal cells – reabsorption of Na^+ and water (ADH), secretion of K^+

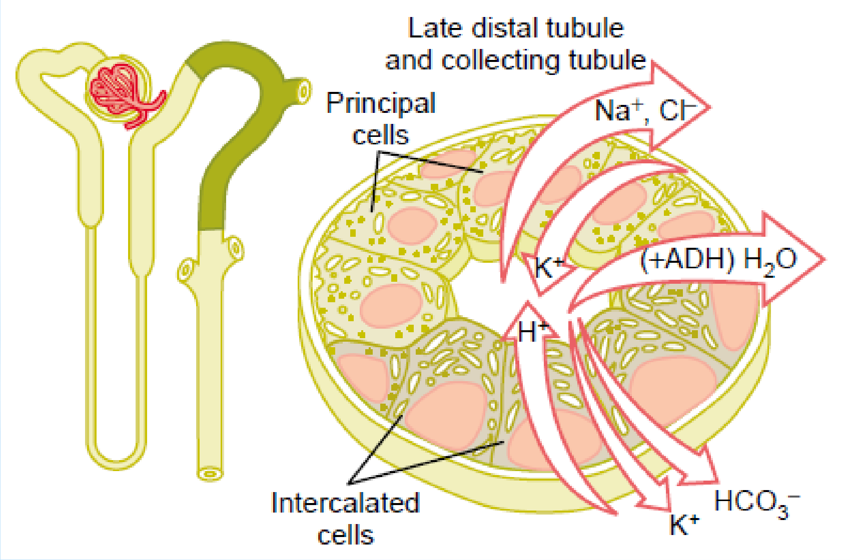


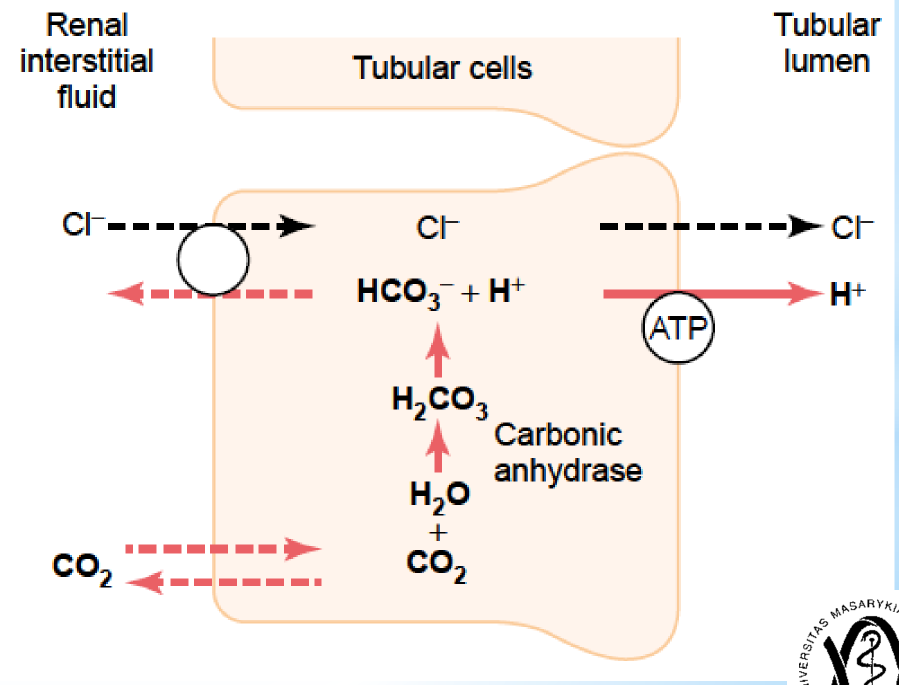


Urine Formation – Tubular Processes

Collecting duct (+ end of distal tubule)

1) principal cells – reabsorption of Na^+ and water (ADH), secretion of K^+
2) intercalated cells – secretion of H^+, reabsorption of HCO_3^- and K^+

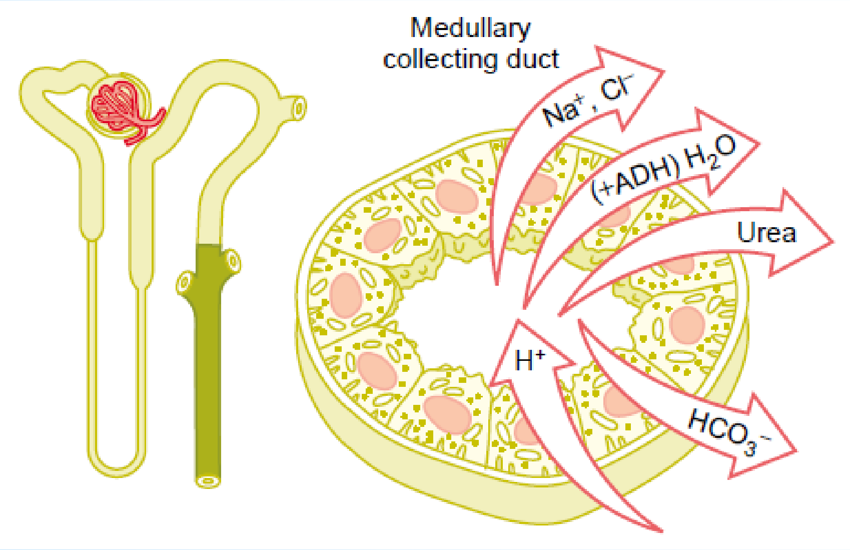




Urine Formation – Tubular Processes

Collecting duct – medullar part

1) reabsorption of Na^+ and Cl^-, water (ADH), urea
2) secretion of H^+, reabsorption of HCO_3^-



Examination of renal function

- Renal clearance
- Examination of function of renal tubules

a) Examination of concentration ability of kidneys

- Concentration test using thirstiness

  (very unpleasant; 12 hours of thirstiness, urine sample every 4 hours – urine density and osmolality; also a blood sample)

- Adiuretin test

  (more pleasant for patient; no drinks and food during night, ADH application in the morning through the nasal mucosa – urine density and osmolality)

a) Examination of dilution ability of kidneys

(test of reaction on increased water intake – decreased ADH production + increased diuresis in healthy people)

Renal Clearance

= the volume of plasma that is completely cleared of the substance by kidneys per unit time

Using *clearance*, we can quantified the excretion ability of kidneys, the velocity of renal blood flow and even basic functions of kidneys (GFR, tubular reabsorption and secretion).

$$C_S \cdot P_S = V \cdot U_S \longrightarrow C_S = \frac{V \cdot U_S}{P_S}$$

[ml/min]

C_S – *clearance* of the substance S

P_S – plasma concentration of the substance S

V – velocity of urine formation

U_S – urine concentrace of the substance S

($V \cdot U_S$ – velocity of urine excretion of the substance S)

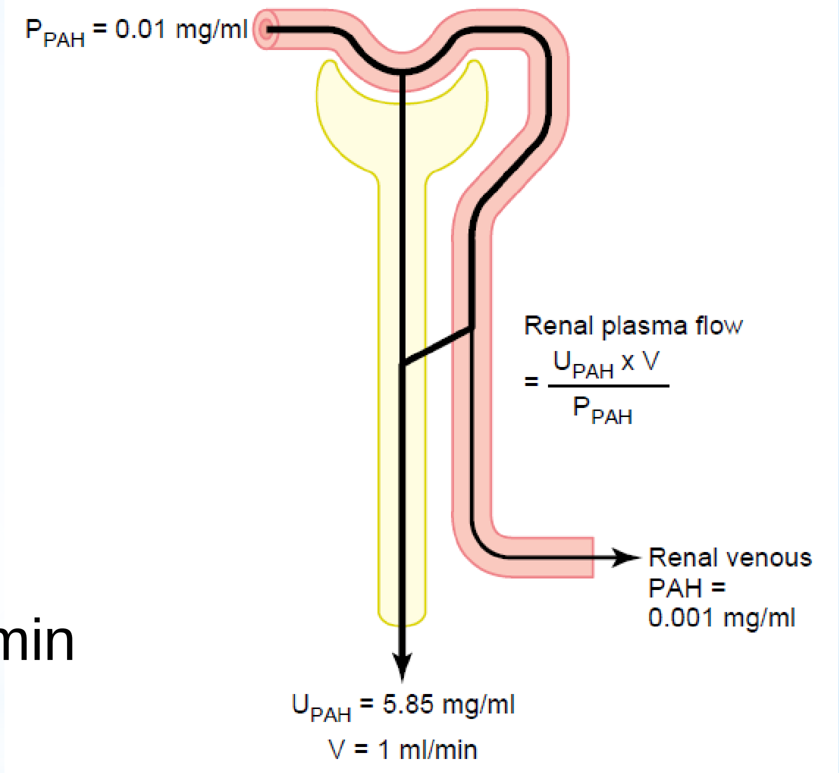
Renal Clearance

Determination of renal plasma flow velocity (RPF)

Clearance of a substance that is fully cleared from plasma in glomerulotubular apparatus.

PAH (paraaminohippuric acid) cleared by 90%

$$RPF = \frac{5.85 \times 1 \text{ mg/min}}{0.01 \text{ mg/ml}} = 585 \text{ ml/min}$$



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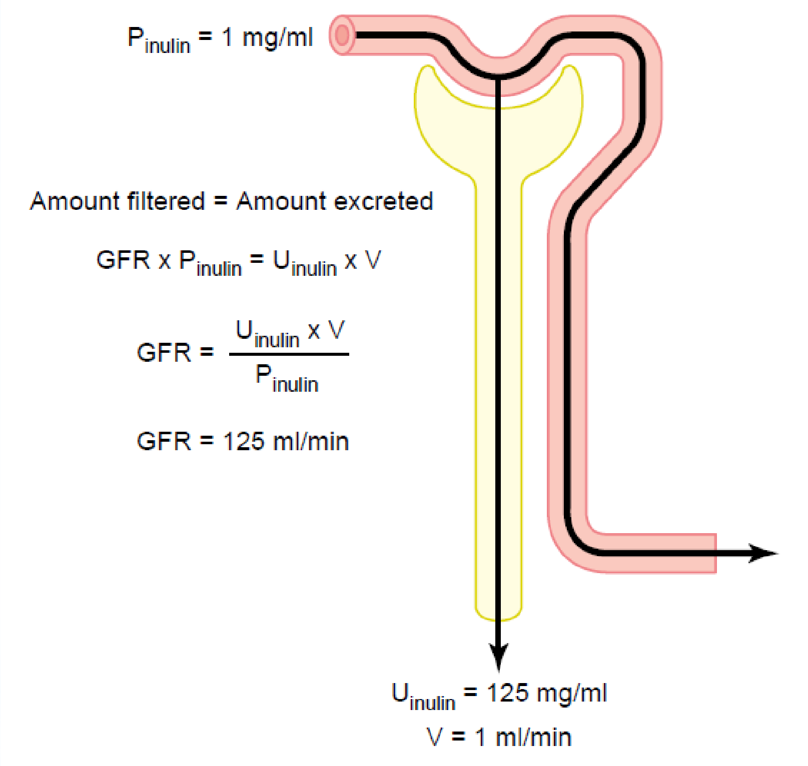
Correction to the extraction ratio of PAH (E_{PAH}):

$$E_{PAH} = \frac{P_{PAH} - V_{PAH}}{P_{PAH}} = 0.9 \longrightarrow RPF = \frac{585 \text{ ml/min}}{0.9} = 650 \text{ ml/min}$$

Renal Clearance

Determination of glomerular filtration rate (GFR)

Clearance of a substance that is fully filtered in the glomerulus and is not reabsorbed/secreted in tubules.



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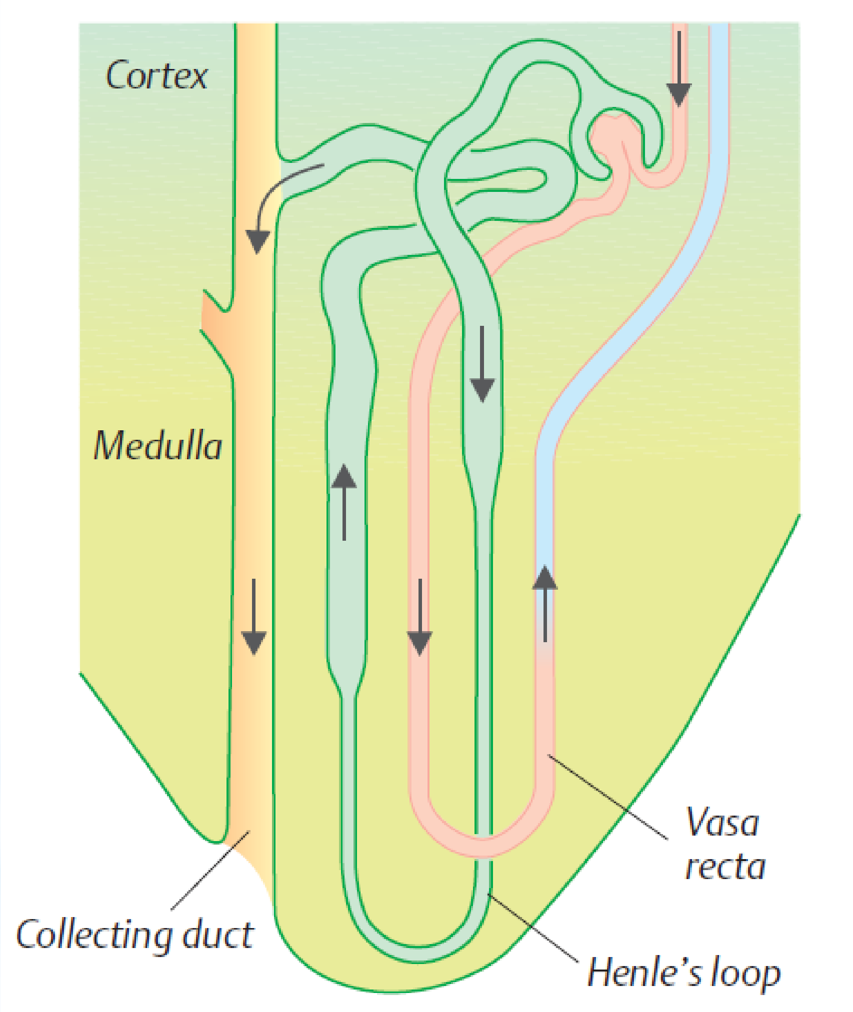
Inulin – polysacharide that is not formed in the body, i.v. application (is present in roots of some plants)

Creatinine – waste product of muscle metabolism, in approximately constant amount in plasma (not necessary to apply i.v.)

The most often estimation of GFR in the clinical practise!

Counter-Current System in Kidneys



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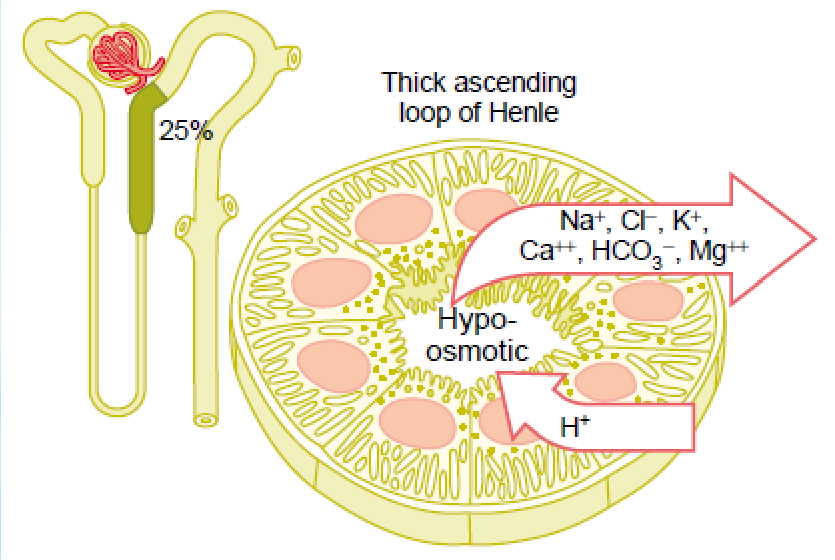
Counter-Current System in Kidneys

Hyperosmotic Renal Medulla – Role of Loop of Henle

1) Active transport of Na^+, co-transport of Na^+ with K^+ and Cl^- from ascending loop of Henle; gradient even 200 mOsm/l
2) Impermeability of ascending loop of Henle for water



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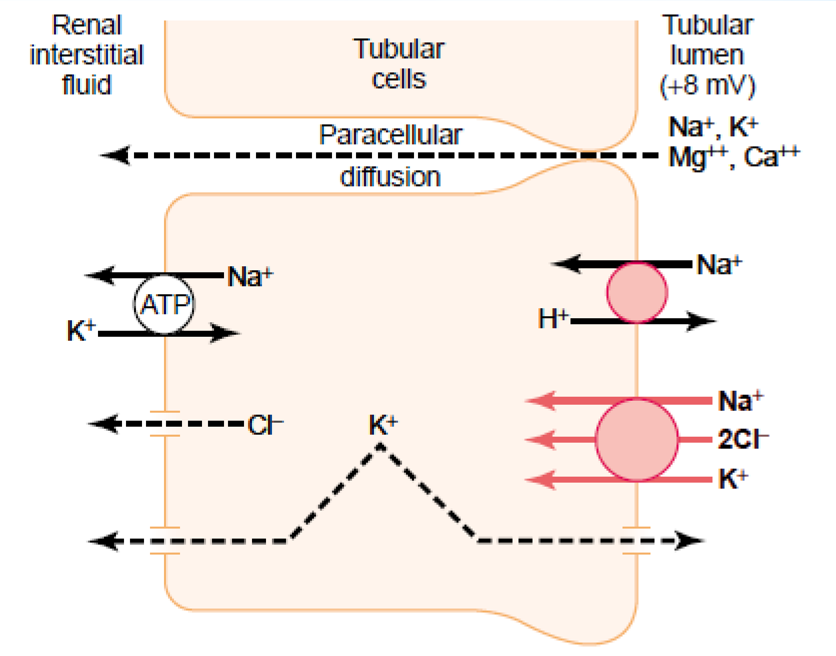
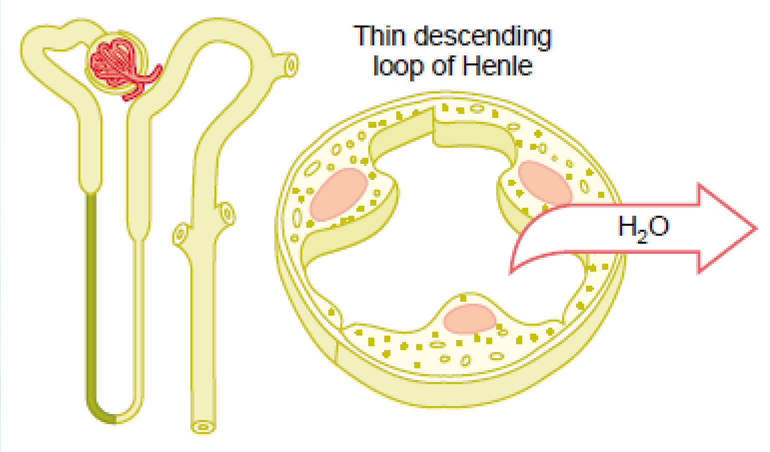


Counter-Current System in Kidneys

Hyperosmotic Renal Medulla – Role of Loop of Henle

1) Active transport of Na^+, co-transport of Na^+ with K^+ and Cl^- from ascending loop of Henle; gradient even 200 mOsm/l
2) Impermeability of ascending loop of Henle for water
3) Permeability of descending loop of Henle for water



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Counter-Current System in Kidneys

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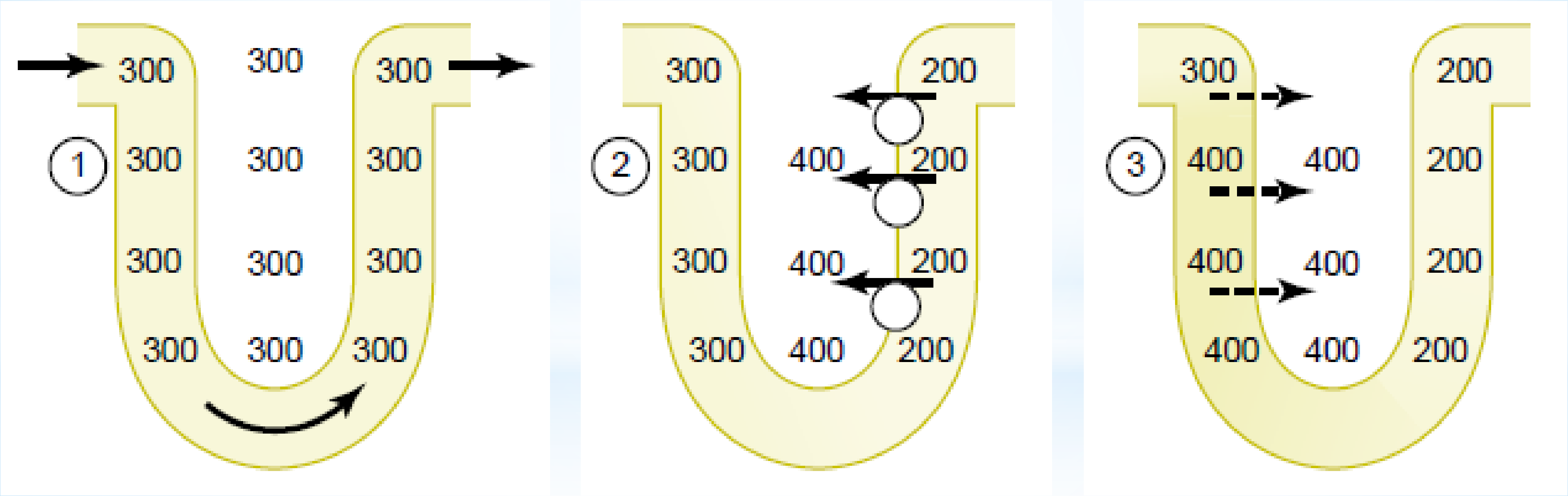
2) Impermeability of ascending loop of Henle for water
3) Permeability of descending loop of Henle for water



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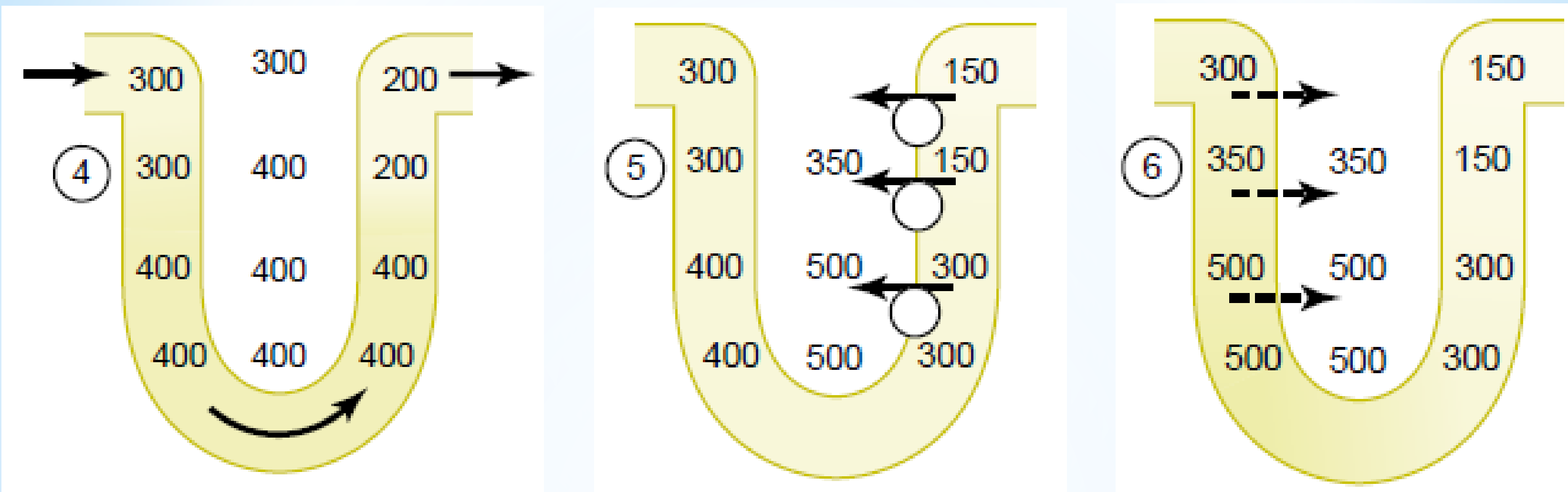
Counter-Current System in Kidneys

Hyperosmotic Renal Medulla – Role of Loop of Henle



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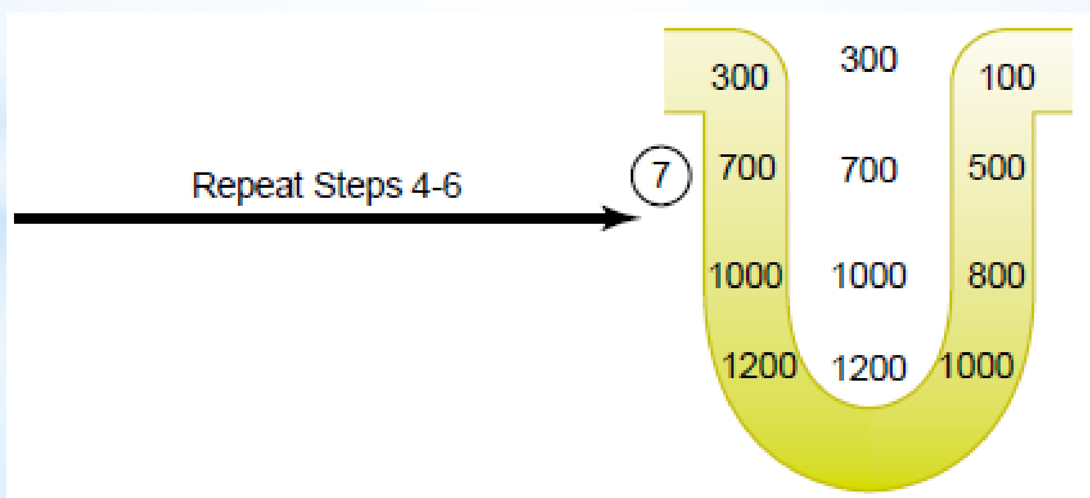
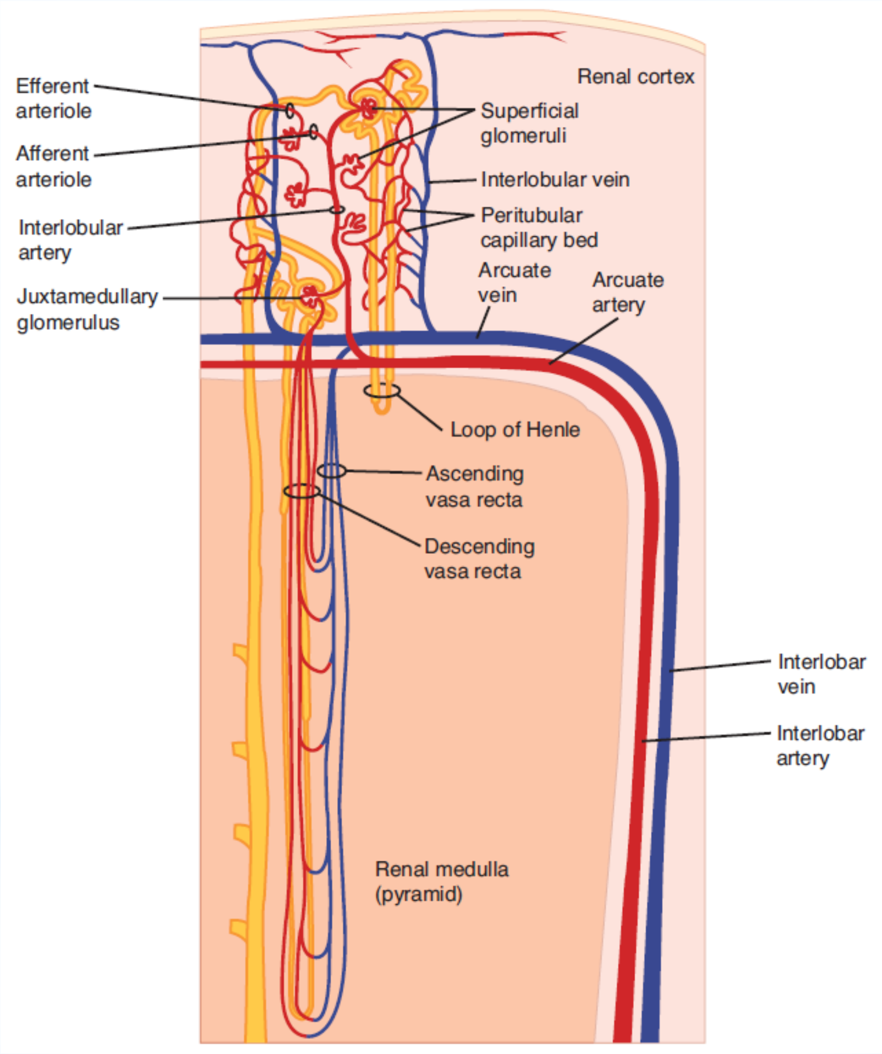


Counter-Current System in Kidneys

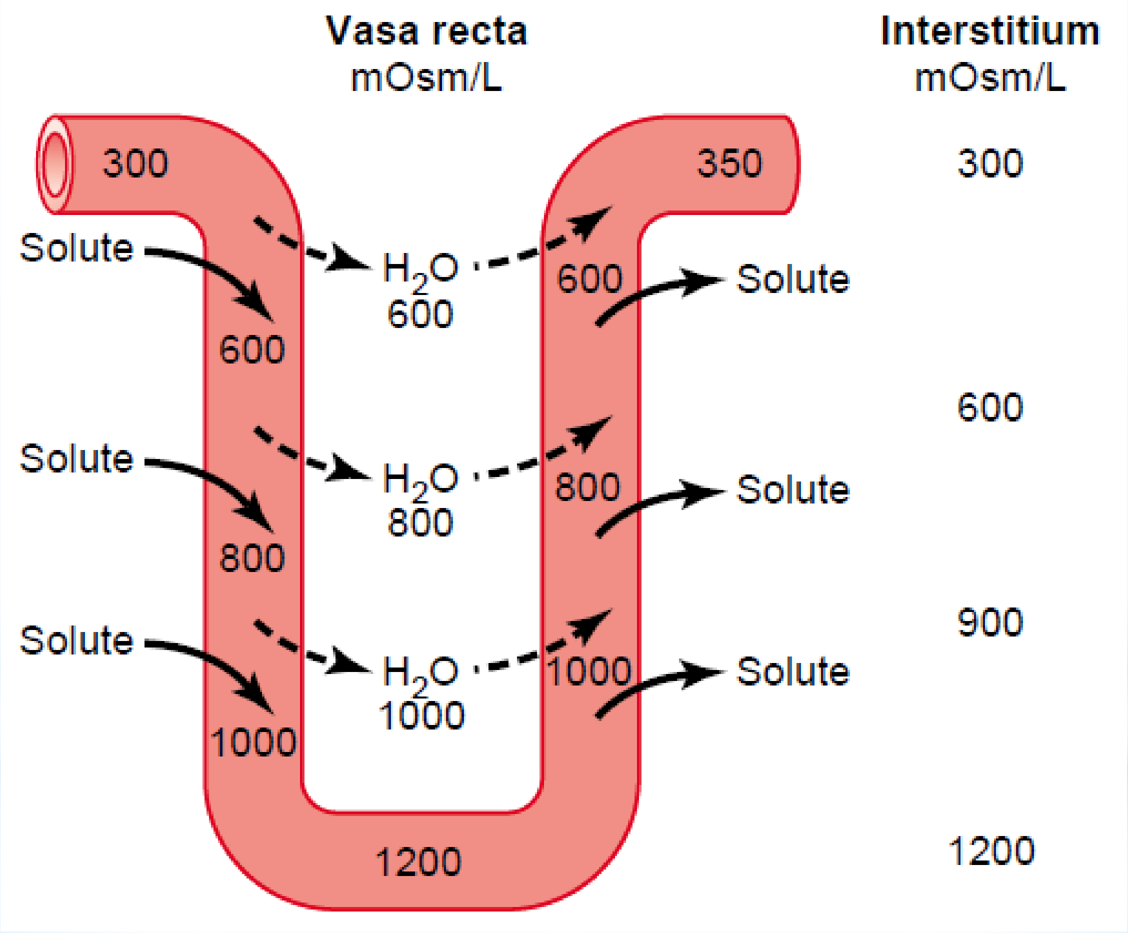
Hyperosmotic Renal Medulla – Role of Vasa Recta



Ganong´s Review of Medical Physiology, 23rd edition

Counter-Current System in Kidneys

Hyperosmotic Renal Medulla – Role of Vasa Recta



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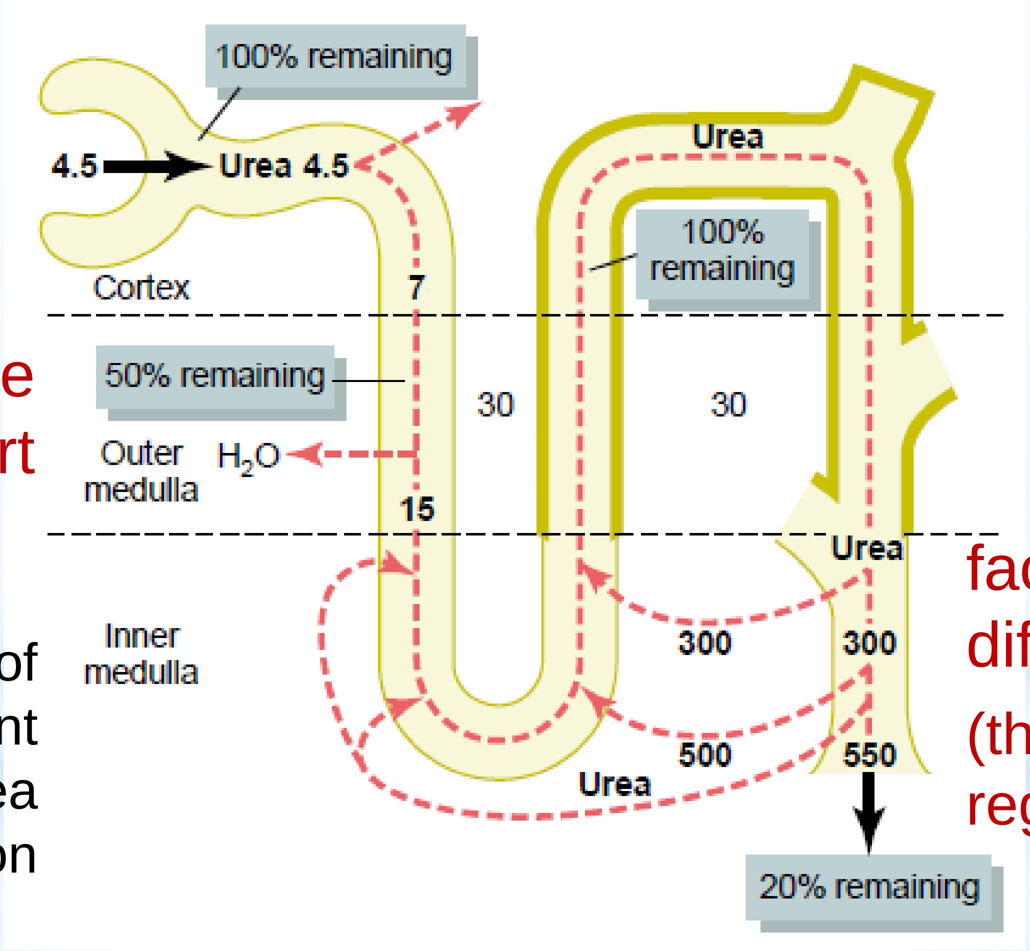
Counter-Current System in Kidneys

Hyperosmotic Renal Medulla – Role of Urea

passive transport

following parts of tubulus resistant to urea reabsorption



facilitated diffusion

(through UT-A1 - regulated by ADH)

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Water Diuresis

- following drinking of a higher amount of hypotonic fluid
- starts ~15 min after drinking, maximum reached within ~40 min
- drinking itself → slightly ↓ ADH secretion
- water reabsorption in the intestine → ↓ plasma osmolarity – osmoreceptors in the hypothalamus → notable ↓ ADH secretion → ↓ water reabsorption in tubulus → ↑ diuresis

Water Diuresis

- following drinking of a higher amount of hypotonic fluid

Water Intoxication

- the water intake per time > the amount of water which can be excreted (maximal diuresis ~16 ml/min)
- hypotonic fluid from plasma to cells $\rightarrow$ cellular edema, symptoms of water intoxication (convulsions, coma even death due to the brain edema)
- iatrogenic – not restricted water intake after application of exogenic ADH or during its higher secretion induced by non-osmotic stimuli (*e.g.* surgery)

Osmotic Diuresis

- induced by presence of non-absorbed osmotically active solutes in renal tubules
- non-absorbed solutes (*e.g.* glucose - *diabetes mellitus*) in the proximal tubules → osmotic effect – water retained in the tubulus

⬇

- ↓ transepithelial gradient for Na^+ (Na^+ in the tubule in a higher amount of water) → inhibition of Na^+ reabsorption in the proximal tubule → Na^+ retained in the tubule ~ further osmotic load → further retaining of water in the tubule

Osmotic Diuresis

- induced by presence of non-absorbed osmotically active solutes in renal tubules

- more isotonic fluid with higher total amount of Na^+ into the loop of Henle → ↓ reabsorption of solutes in the ascendent loop of Henle after reaching the borderline concentration gradient for Na^+ reabsorption → ↓ hypertonicity of the renal medulla

- more fluid flows through other parts of tubulus + ↓ hypertonicity of the renal medulla → ↓ water reabsorption in the collecting duct → ↑ diuresis, urine with an increased amount of solutes